```
L2      STRUCTURE UPLOADED

=> s l2
SEARCH FAILED DUE TO A STRUCTURE QUERY ERROR
The structure query could not be searched.  Please review and revise
your structure query, especially checking the variable definitions
and
attachments. In rare instances the failure may be due to a system
problem. Please contact your local STN Help Desk if you need
assistance.

=> s l2 sss
SEARCH FAILED DUE TO A STRUCTURE QUERY ERROR
The structure query could not be searched.  Please review and revise
your structure query, especially checking the variable definitions
and
attachments. In rare instances the failure may be due to a system
problem. Please contact your local STN Help Desk if you need
assistance.

=>

---Logging off of STN---


=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                            SINCE FILE
TOTAL
                                                    ENTRY
SESSION
FULL ESTIMATED COST                                  9.24
9.45

STN INTERNATIONAL LOGOFF AT 14:01:24 ON 04 AUG 2004



Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1653adk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2
```

```
* * * * * * * * * *  Welcome to STN International  * * * * * * * *
* *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12  BEILSTEIN enhanced with new display and select
options,
                  resulting in a closer connection to BABS
 NEWS  4  Jul 30  BEILSTEIN on STN workshop to be held August 24 in
conjunction
                  with the 228th ACS National Meeting
 NEWS  5  AUG 02  IFIPAT/IFIUDB/IFICDB reloaded with new search and
display
                  fields
 NEWS  6  AUG 02  CAplus and CA patent records enhanced with European
and Japan
                  Patent Office Classifications
 NEWS  7  AUG 02  The Analysis Edition of STN Express with Discover!
                  (Version 7.01 for Windows) now available
 NEWS  8  AUG 04  Pricing for the Save Answers for SciFinder Wizard
within
                  STN Express with Discover! will change September 1,
2004
 NEWS  9  AUG 27  BIOCOMMERCE: Changes and enhancements to content
coverage
 NEWS 10  AUG 27  BIOTECHABS/BIOTECHDS: Two new display fields added
for legal
                  status data from INPADOC
 NEWS 11  SEP 01  INPADOC: New family current-awareness alert (SDI)
available
 NEWS 12  SEP 01  New pricing for the Save Answers for SciFinder
Wizard within
                  STN Express with Discover!
 NEWS 13  SEP 01  New display format, HITSTR, available in
WPIDS/WPINDEX/WPIX
 NEWS 14  SEP 14  STN Patent Forum to be held October 13, 2004, in
Iselin, NJ

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to
STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  of commercial gateways or other similar uses is prohibited and may
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  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *
* *

FILE 'HOME' ENTERED AT 14:21:11 ON 23 SEP 2004

=> FIL REGISTRY
COST IN U.S. DOLLARS                            SINCE FILE
TOTAL
                                                    ENTRY
SESSION
FULL ESTIMATED COST                                  0.21
0.21

FILE 'REGISTRY' ENTERED AT 14:21:16 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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provided by InfoChem.

STRUCTURE FILE UPDATES:   22 SEP 2004  HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES:  22 SEP 2004  HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for
details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=> screen 2043

L1    SCREEN CREATED

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Uploading H:\STN queries\10075097c.str
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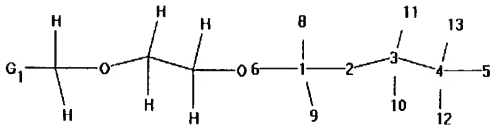


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chain nodes :
1  2  3  4  5  6  8  9  10  11  12  13
chain bonds :
1-2  1-6  1-8  1-9  2-3  3-4  3-10  3-11  4-5  4-12  4-13
exact/norm bonds :
1-2  1-6  2-3  4-5
exact bonds :
1-8  1-9  3-4  3-10  3-11  4-12  4-13


G1:C,O,S,N

Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  8:CLASS
9:CLASS  10:CLASS  11:CLASS  12:CLASS  13:CLASS



L2      STRUCTURE UPLOADED

=> que L2 AND L1

L3   QUE L2 AND L1

=> s l3 fam sam
STRUCTURES CONTAINING VARIABLE NODES NOT VALID IN EXACT OR FAMILY
SEARCH
You have requested a full structure (EXA or FAM) search on a
structure containing one of the special variable-atom symbols
A, M, Q, or X, or a variable group G.  Only bond variability
is allowed in structures for EXA or FAM searches.  Variable
nodes are never permitted.

=> s l3 ful
FULL SEARCH INITIATED 14:21:42 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 203457 TO ITERATE

100.0% PROCESSED  203457 ITERATIONS                      64914
ANSWERS
SEARCH TIME: 00.00.02

L4        64914 SEA SSS FUL L2 AND L1

=> file caplus
COST IN U.S. DOLLARS                            SINCE FILE
TOTAL
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                                                    ENTRY
SESSION
FULL ESTIMATED COST                                 155.42
155.63

FILE 'CAPLUS' ENTERED AT 14:21:51 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 23 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004  (20040922/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> l4
L5       71947 L4

=> l5 and insulin
        166064 INSULIN
          5184 INSULINS
        166144 INSULIN
                 (INSULIN OR INSULINS)
L6         287 L5 AND INSULIN

=> l6 and english/la
      13699382 ENGLISH/LA
L7         245 L6 AND ENGLISH/LA

=> l7 and patent/dt
       4436326 PATENT/DT
L8         136 L7 AND PATENT/DT

=> l7 not l8
L9         109 L7 NOT L8

=> l8 and pd<20010215
      21338416 PD<20010215
                 (PD<20010215)
L10         74 L8 AND PD<20010215

=> d l10 1-5 hitstr ibib
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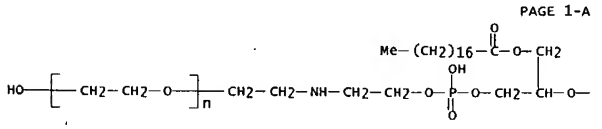
L10 ANSWER 1 OF 74 CAPLUS COPYRIGHT 2004 ACS on STN
IT 145035-96-7, DSPE-PEG
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(hydrogel-isolated cochleate formulations and their use for the delivery of biol. relevant mols.)
RN 145035-96-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[7-hydroxy-7-oxido-13-oxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-yl]-ω-hydroxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

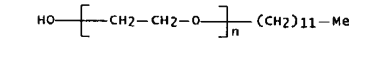
ACCESSION NUMBER: 2003:544700 CAPLUS Full-text
DOCUMENT NUMBER: 139:106457
TITLE: Hydrogel-isolated cochleate formulations and their use for the delivery of biologically relevant molecules
INVENTOR(S): Zarif, Leila; Jin, Tuo; Segarra, Ignacio; Mannino, Raphael J.
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA; University of Medicine and Dentistry of New Jersey
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. Ser. No. 235,400.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6592894	B1	20030715	US 2000-613840	20000711
US 6153217	A	20001128	US 1999-235400	19990122 <--
WO 2001052817	A2	20010726	WO 2001-US2299	20010124
WO 2001052817	A3	20020221		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1259224	A2	20021127	EP 2001-903273	20010124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003529557	T2	20031007	JP 2001-552865	20010124
US 2003228355	A1	20031211	US 2003-421358	20030423

PRIORITY APPLN. INFO.:
US 1999-235400 A2 19990122
WO 2000-US1684 W 20000124
US 2000-613840 A 20000711
WO 2001-US2299 W 20010124
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 74 CAPLUS COPYRIGHT 2004 ACS on STN
IT 9002-92-0, Polidocanol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pressurized container having an aerosolized pharmaceutical composition)
RN 9002-92-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



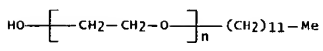
ACCESSION NUMBER: 2001:828918 CAPLUS Full-text
DOCUMENT NUMBER: 135:362585
TITLE: Pressurized container having an aerosolized pharmaceutical composition
INVENTOR(S): Modi, Pankaj
PATENT ASSIGNEE(S): Generex Pharmaceuticals, Inc., Can.
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 272,563.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6315984	B1	20011113	US 1999-388344	19990903
US 6350432	B1	20020226	US 1999-272563	19990319
WO 2000056291	A1	20000928	WO 2000-CA260	20000310 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1162958	A1	20011219	EP 2000-908880	20000310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539240	T2	20021119	JP 2000-606197	20000310
NZ 514319	A	20021126	NZ 2000-514319	20000310
AU 766745	B2	20031023	AU 2000-31400	20000310

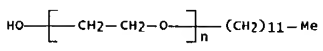
PRIORITY APPLN. INFO.:
US 1999-272563 A2 19990319
US 1999-388344 A 19990903
WO 2000-CA260 W 20000310

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

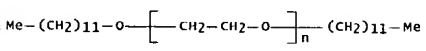
L10 ANSWER 3 OF 74 CAPLUS COPYRIGHT 2004 ACS on STN
IT 9002-92-0, Polyoxyethylene lauryl ether 9002-92-0D, Polidocanol, alkyl ethers 57208-34-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerosol formulations for buccal and pulmonary application)
RN 9002-92-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 9002-92-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 57208-34-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-(dodecyloxy)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:808253 CAPLUS Full-text
DOCUMENT NUMBER: 135:348902
TITLE: Aerosol formulations for buccal and pulmonary application
INVENTOR(S): Modi, Pankaj
PATENT ASSIGNEE(S): Generex Pharmaceuticals Incorporated, Can.
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 251,464.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6312665	B1	20011106	US 1999-386284	19990831
US 6436367	B1	20020820	US 1999-251464	19990217
WO 2000037051	A1	20000629	WO 1999-CA1231	19991216 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140019	A1	20011010	EP 1999-962009	19991216
EP 1140019	B1	20030625		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532536	T2	20021002	JP 2000-589162	19991216
NZ 512188	A	20021025	NZ 1999-512188	19991216
AU 760445	B2	20030515	AU 2000-18518	19991216
AT 243498	E	20030715	AT 1999-962009	19991216
EP 1338272	A1	20030827	EP 2003-2417	19991216
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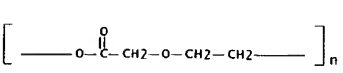
PT 1140019	T	20031031	PT 1999-962009	19991216
ES 2203227	T3	20040401	ES 1999-962009	19991216
US 6375975	B1	20020423	US 2000-519285	20000306
US 6451286	B1	20020917	US 2000-574504	20000519
US 2003035831	A1	20030220	US 2002-222699	20020816
US 2003157029	A1	20030821	US 2002-222240	20020816

PRIORITY APPLN. INFO.:

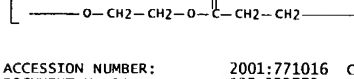
US 1998-113239P	P	19981221
US 1999-251464	A2	19990217
US 1999-386284	A	19990831
EP 1999-962009	A3	19991216
WO 1999-CA1231	W	19991216
US 2000-519285	A2	20000306
US 2000-574504	A2	20000519

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 74 CAPLUS COPYRIGHT 2004 ACS on STN
IT 31621-87-1, Poly(p-dioxanone), SRU 121425-79-4
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymeric foam/fiber composite for repair or regeneration of tissue)
RN 31621-87-1 CAPLUS
CN Poly[oxy(1-oxo-1,2-ethanediyl)oxy-1,2-ethanediyl] (9CI) (CA INDEX NAME)



RN 121425-79-4 CAPLUS
CN Poly[oxy-1,2-ethanediyloxy(1-oxo-1,3-propanediyl)] (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:771016 CAPLUS Full-text
DOCUMENT NUMBER: 135:322772
TITLE: Polymer-based foam composite for the repair or regeneration of tissue
INVENTOR(S): Vyakarnam, Murty N.; Zimmerman, Mark C.; Scopelianos, Angelo George; Chun, Iksoo; Melican, Mora C.; Bazilio, Clairene A.; Roller, Mark B.; Gorky, David V.
PATENT ASSIGNEE(S): Ethicon, Inc., USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 345,096.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6306424	B1	20011023	US 1999-469118	19991221
US 6333029	B1	20011225	US 1999-345096	19990630
CA 2313067	AA	20001230	CA 2000-2313067	20000629 <--
AU 2000043758	A5	20010222	AU 2000-43758	20000629
EP 1064958	A1	20010103	EP 2000-305501	20000630 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001049018	A2	20010220	JP 2000-199398	20000630
EP 1452191	A2	20040901	EP 2004-76136	20000630
EP 1452191	A3	20040922		
R: DE, FR, GB, IT				
US 2001033857	A1	20011025	US 2000-740086	20001219
US 6365149	B2	20020402		
US 6534084	B1	20030318	US 2000-740289	20001219
EP 1234587	A1	20020828	EP 2001-301703	20010226
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US 2003077311	A1	20030424	US 2001-938364	20010824

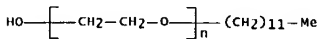
PRIORITY APPLN. INFO.:

US 1999-345096	A2	19990630
US 1999-469118	A	19991221
EP 2000-305501	A3	20000630
CA 2001-2338440	A	20010227

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES

AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 74 CAPLUS COPYRIGHT 2004 ACS on STN
IT 9002-92-0, brij-35
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition; preparation of lipophilic human glucagon-like peptide-1 derivs. with protracted action profiles)
RN 9002-92-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:566665 CAPLUS Full-text
DOCUMENT NUMBER: 135:122756
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 265,141.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
WO 9808871	A1	19980305	WO 1997-DK340	19970822 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

JP 2001011095	A2	20010116	JP 2000-152778	19970822 <--
ZA 9707791	A	19980302	ZA 1997-7791	19970829 <--
ZA 9707828	A	19980302	ZA 1997-7828	19970901 <--
US 6268343	B1	20010731	US 1999-258750	19990226
US 6384016	B1	20020507	US 1999-265141	19990308
US 2002025933	A1	20020228	US 2001-908534	20010718
US 2003199672	A1	20031023	US 2002-285079	20020819
US 2004127418	A1	20040701	US 2003-730215	20031208

PRIORITY APPLN. INFO.:		
DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
US 1998-84357P	P	19970822
WO 1997-DK340	W	19970822
US 1997-918810	B2	19970826
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
US 1998-38432	B2	19980311
US 1998-78422P	P	19980318
US 1998-82478P	P	19980421
US 1998-82479P	P	19980421
US 1998-82480P	P	19980421
US 1998-82802P	P	19980423
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308
US 1997-35904P	P	19970124
US 1997-35905P	P	19970124
JP 1998-511183	A3	19970822
US 1997-922200	B2	19970902
DK 1998-271	A	19980227
DK 1998-272	A	19980227
DK 1998-274	A	19980227
EP 1998-610006	A	19980313
DK 1998-507	A	19980408
DK 1998-508	A	19980408
DK 1998-509	A	19980408
US 1998-85789P	P	19980518
US 1999-258187	B1	19990225
US 1999-398111	A1	19990916
US 2001-908534	A1	20010718

OTHER SOURCE(S): MARPAT 135:122756

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L2 STRUCTURE UPLOADED
L3 QUE L2 AND L1
L4 64914 S L3 FUL

FILE 'CAPLUS' ENTERED AT 14:21:51 ON 23 SEP 2004
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L7 245 L6 AND ENGLISH/LA
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=> l11 and conjugate
57997 CONJUGATE
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89365 CONJUGATE
(CONJUGATE OR CONJUGATES)
L12 24 L11 AND CONJUGATE

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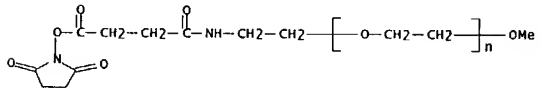
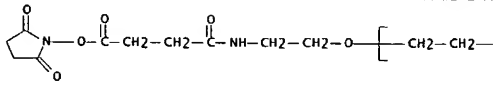
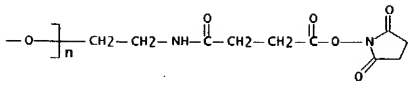
L12 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 92451-00-8P 186020-53-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(covalent attachment of insulin to biodegradable diblock copolymers)
RN 92451-00-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



RN 186020-53-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethyl]-ω-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

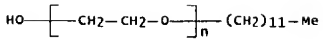




ACCESSION NUMBER: 2002:346863 CAPLUS Full-text
DOCUMENT NUMBER: 138:95323
TITLE: Towards the covalent attachment of insulin to biodegradable diblock copolymers
AUTHOR(S): Tessmar, J.; Mikos, A.; Gopferich, A.
CORPORATE SOURCE: Pharmaceutical Technology, University of Regensburg, Regensburg, 93040, Germany
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 331-332. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
Insulin was used as a model substance to establish the covalent attachment of proteins to hydrophilic biodegradable diblock copolymer surfaces. Expts. conducted with amine reactive succinimidyl esters of poly(ethylene glycol) [PEG-SE], which represent the protein binding anchor of the polymers in question, confirmed that the covalent binding of insulin to PEG-SE can be used for the immobilization of insulin on polymer surfaces.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 9002-92-0, brij-35
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition; preparation of lipophilic human glucagon-like peptide-1 derivs. with protracted action profiles)
RN 9002-92-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:566665 CAPLUS Full-text
DOCUMENT NUMBER: 135:122756
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 265,141.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
WO 9808871	A1	19980305	WO 1997-DK340	19970822 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822 <--
ZA 9707791	A	19980302	ZA 1997-7791	19970829 <--
ZA 9707828	A	19980302	ZA 1997-7828	19970901 <--
US 6268343	B1	20010731	US 1999-258750	19990226
US 6384016	B1	20020507	US 1999-265141	19990308
US 2002025933	A1	20020228	US 2001-908534	20010718
US 2003199672	A1	20031023	US 2002-285079	20020819
US 2004127418	A1	20040701	US 2003-730215	20031208

PRIORITY APPLN. INFO.:

DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
US 1998-84357P	P	19970822
WO 1997-DK340	W	19970822
US 1997-918810	B2	19970826
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
US 1998-38432	B2	19980311
US 1998-78422P	P	19980318
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US 1998-82479P	P	19980421
US 1998-82480P	P	19980421
US 1998-82802P	P	19980423
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308
US 1997-35904P	P	19970124
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JP 1998-511183	A3	19970822
US 1997-922200	B2	19970902
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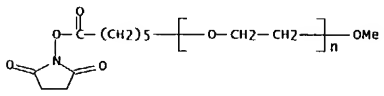
DK 1998-272	A	19980227
DK 1998-274	A	19980227
EP 1998-610006	A	19980313
DK 1998-507	A	19980408
DK 1998-508	A	19980408
DK 1998-509	A	19980408
US 1998-85789P	P	19980518
US 1999-258187	B1	19990225
US 1999-398111	A1	19990916
US 2001-908534	A1	20010718

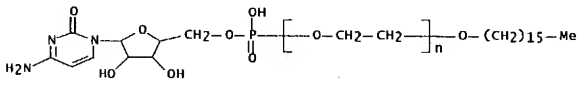
OTHER SOURCE(S): MARPAT 135:122756
ABSTRACT:
The present invention relates to pharmaceutical compns. comprising lipophilic human glucagon-like peptide-1 (GLP-1) derivs. having a lipophilic substituent and a surfactant. Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (preparation given), followed by deesterification with CF3CO2H and chromatog. purification gave 8% bis-adduct Lys[Me(CH2)12CO-γ-Glu]26,34-GLP-1(7-37)-OH. Several prepared lipophilic GLP-1 analogs were tested for protracted plasma concentration in pigs and were found to be much more persistent than GLP-1(7-37). In addition, the time of peak plasma concentration was found to vary within wide limits depending on the particular lipophilic GLP-1 derivative selected. The efficacy of several prepared derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

L12 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 212969-35-2P 326892-08-4P 326892-09-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydrophilic and lipophilic balanced microemulsions of free

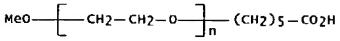
and/or
conjugated drugs such as insulin)
RN 212969-35-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-
oxohexyl]-ω-methoxy- (9CI) (CA INDEX NAME)



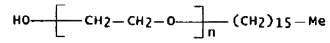
RN 326892-08-4 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-(hexadecyloxy)-, ester with 4-amino-1-(5'-O-phosphono-β-D-arabinofuranosyl)-2(1H)-pyrimidinone (1:1) (9CI) (CA INDEX NAME)



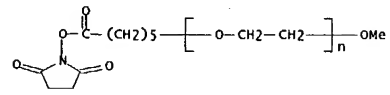
RN 326892-09-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(5-carboxypentyl)-ω-methoxy- (9CI) (CA INDEX NAME)



IT 9004-95-9DP, Polyoxyethylene cetyl ether, conjugates with tri-Bu AraCMP 212969-35-2DP, conjugates with hexyl insulin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hydrophilic and lipophilic balanced microemulsions of free and/or
conjugated drugs such as insulin)
RN 9004-95-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hexadecyl-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 212969-35-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-
oxohexyl]-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2001:131193 CAPLUS Full-text
DOCUMENT NUMBER: 134:183490
TITLE: Hydrophilic and lipophilic balanced microemulsion formulations of free-form and/or conjugation-stabilized therapeutic agents such as insulin
INVENTOR(S): Ekwuribe, Nnochiri Nkem; Ramaswamy, Muthukumar; Radhakrishnan, Balasingam; Allaudeen, Hameedsulthan S.
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: U.S., 32 pp., Cont.-in-part of U. S. 5,681,811.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

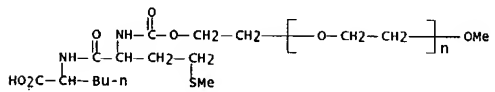
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6191105	B1	20010220	US 1997-958383	19971027
US 5359030	A	19941025	US 1993-59701	19930510 <--
US 5438040	A	19950801	US 1994-276890	19940719 <--
US 5681811	A	19971028	US 1995-509422	19950731 <--
US 2003229006	A1	20031211	US 2003-448524	20030530
US 2003229010	A1	20031211	US 2003-448535	20030602

PRIORITY APPLN. INFO.: US 1993-59701 A3 19930510
US 1994-276890 A2 19940719
US 1995-509422 A2 19950731
US 1997-958383 A3 19971027
US 2000-614203 A1 20000712

ABSTRACT:
A therapeutic formulation comprising a microemulsion of a therapeutic agent in free and/or conjugate coupled form, wherein the microemulsion comprises a water-in-oil (w/o) microemulsion including a lipophilic phase and a hydrophilic phase, and has a hydrophilic and lipophilic balance (HLB) value between 3 and 7 is described. The therapeutic agent is selected from the group consisting of insulin, calcitonin, ACTH, glucagon, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic releasing factors, prolactin, thyroid stimulating hormones, endorphins, enkephalins, vasopressin, non-naturally occurring opioids, superoxide dismutase, interferon, asparaginase, arginase, arginine deaminase, adenosine deaminase, RNase, trypsin, chymotrypsin, papain, Ara-A (Arabinofuranosyladenine), acylguanosine, nordeoxyguanosine, azidothymidine, dideoxyadenosine, dideoxycytidine, dideoxyinosine, floxuridine, 6-mercaptopurine, doxorubicin, daunorubicin, or I-darubicin, erythromycin, vancomycin, oleandomycin, ampicillin, quinidine and heparin. In a particular aspect, the invention comprises an insulin composition suitable for parenteral as well as non-parenteral administration, preferably oral or parenteral administration, comprising insulin covalently coupled with a polymer including (i) a linear polyalkylene glycol moiety and (ii) a lipophilic moiety, wherein the insulin, the linear polyalkylene glycol moiety and the lipophilic moiety are conformationally arranged in relation to one another such that the insulin in the composition has an enhanced in vivo resistance to enzymic degradation, relative to insulin alone. The microemulsion compns. of the invention are usefully employed in therapeutic as well as non-therapeutic, e.g., diagnostic, applications. For example, a microemulsion formulation was prepared containing Capmul MCM 53.0, Centrophase 31 5.7, propylene glycol 19.9, Tween 80 1.4, hexyl insulin in NaP buffer 15 mg/mL, and NaP buffer up to 100%, resp. Also, preparation of hexyl ***insulin*** conjugates with Me (ethylene glycol)7-O-hexanoic acid was carried out.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 329024-07-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(PEGs for peptide and protein modification for identification of PEGylation site)
RN 329024-07-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, 1-ester with N-carboxy-L-methionyl-L-norleucine (9CI) (CA INDEX NAME)

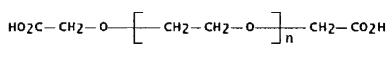


ACCESSION NUMBER: 2001:38765 CAPLUS Full-text
DOCUMENT NUMBER: 134:204694
TITLE: New PEGs for peptide and protein modification, PEGylation site suitable for identification of the
AUTHOR(S): Veronese, F. M.; Sacca, B.; de Laureto, P. Polverino; Sergi, M.; Caliceti, P.; Schiavon, O.; Orsolini, P.
CORPORATE SOURCE: Department of Pharmaceutical Sciences (CNR Center for Chemical Investigation of Drugs), University of Padova, Padua, 35131, Italy
SOURCE: Bioconjugate Chemistry (2001), 12(1), 62-70
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

New PEG derivs. were studied for peptide and protein modification, based upon
an amino acid arm, Met-Nle or Met-βAla, activated as succinimidyl ester.
PEG-Met-Nle-OSu or PEG-Met-βAla-OSu react with amino groups in protein-yielding conjugates with stable amide bond. From these
conjugates PEG may be removed by BrCN treatment, leaving Nle or
βAla as reporter amino acid, at the site where PEG was bound. The conjugation of PEG and its removal by BrCN treatment was assessed on a partial
sequence of glucagone and on lysozyme as model peptide or protein. Furthermore,
insulin , a protein with three potential sites of PEGylation, was
modified by PEG-Met-Nle, and the PEG isomers were separated by HPLC. After removal
of PEG, as reported above, the sites of PEGylation were identified by characterization of the two insulin chains obtained after reduction and
carboxymethylation. Mass spectrometry, amino acid anal. and Edman sequence,
could reveal the position of the reporter norleucine that corresponds to the
position of PEG binding.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 39927-08-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(functionalized poly(propylene fumarate) and poly(propylene fumarate-co-ethylene glycol) for coupling to biomols.)
RN 39927-08-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-(carboxymethoxy)- (9CI) (CA INDEX NAME)



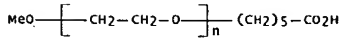
ACCESSION NUMBER: 2000:756475 CAPLUS Full-text
DOCUMENT NUMBER: 133:325635
TITLE: Functionalized poly(propylene fumarate) and poly(propylene fumarate-co-ethylene glycol)
INVENTOR(S): Mikos, Antonios G.; Jo, Seongbong
PATENT ASSIGNEE(S): Wm. Marsh Rice University, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000062630	A1	20001026	WO 2000-US10139	20000414 <--
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1171006	A1	20020116	EP 2000-923381	20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002022676	A1	20020221	US 2000-550372	20000414
US 6384105	B1	20020507		
US 6423790	B1	20020723	US 2000-549485	20000414
JP 2002542339	T2	20021210	JP 2000-611774	20000414
AU 760358	B2	20030515	AU 2000-43518	20000414 <--
AU 2000043518	A5	20001102		
US 2002177668	A1	20021128	US 2002-127117	20020422
US 6759485	B2	20040706		

PRIORITY APPLN. INFO.: US 1999-129577P P 19990416
US 1999-146991P P 19990803
US 1999-167328P P 19991124
US 1999-167388P P 19991124
US 2000-549485 A3 20000414
WO 2000-US10139 W 20000414
ABSTRACT:
Poly(ethylene glycol) (PEG), a highly biocompatible hydrophilic polyether, is
tethered to poly(propylene fumarate) (PPF), a biodegradable polyester. To
avoid change in mol. weight distribution of PPF, end hydroxyl groups of PPF are
reacted with bis-carboxymethyl PEG after being treated with thionyl chloride.
New end carboxyl groups of the PEG-tethered PPF are further reacted with
N-hydroxysuccinimide (NHS) in the presence of dicyclohexylcarbodiimide (DCC) to
couple bioactive mols. Glutamine and glycine-arginine-glycine-aspartic acid
(GRGD) are attached to the PEG-tethered PPF in 50 mM phosphate buffer of pH of
7.4. The method is valuable for the preparation of a triblock copolymer with PEG
end blocks and the coupling of biol. active mols.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

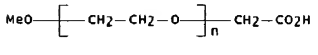
L12 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 326892-09-5D, conjugates with human insulin
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(stability and phys. characteristics of orally active amphiphilic human
insulin analog, methoxy(polyethylene glycol) hexanoyl human recombinant insulin)
RN 326892-09-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(5-carboxypentyl)-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2000:672439 CAPLUS Full-text
DOCUMENT NUMBER: 134:212549
TITLE: Stability and physical characteristics of orally
active amphiphilic human insulin analog, methoxy (polyethylene glycol) hexanoyl human recombinant insulin (HIM2)
AUTHOR(S): Krishnan, B. Radha; Rajagopalan, J. S.; Burnham, J.
CORPORATE SOURCE: Protein Delivery Inc., Durham, NC, 27713, USA
SOURCE: Proceedings of the International Symposium on
Controlled Release of Bioactive Materials (2000), 27th, 1038-1039
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Orally active HIM2, an amphiphilic oligomer attached to B29-Lys of human
insulin , showed significant thermal stability in aqueous buffer and in
solid state over unmodified insulin. The change in pI value as the result of modification at B29-Lys suggests that the dissoln. and solubility profile
of HIM2 would be different from that of insulin in the gastrointestinal tract. The chemical modification contributed to a concurrent
increase in hydrodynamic radius of insulin but unaltered the self-association state (monomeric) of insulin at low protein concentration

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

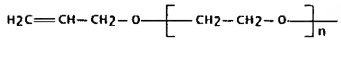
L12 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 67665-18-3 112311-92-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(polymeric delivery agents comprising polymer conjugated to modified
amino acid or derivative thereof)
RN 67665-18-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-methoxy- (9CI) (CA INDEX NAME)



RN 112311-92-9 CAPLUS
CN 2,5-Furandione, polymer with α-methyl-ω-(2-propenyloxy)poly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

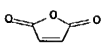
CM 1

CRN 27252-80-8
CMF (C2 H4 O)n C4 H8 O
CCI PMS

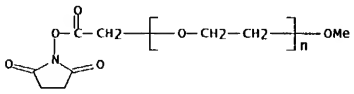


CM 2

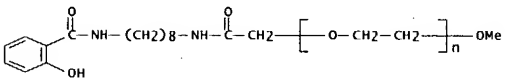
CRN 108-31-6
CMF C4 H2 O3



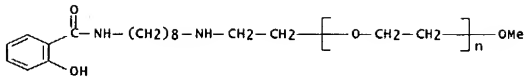
IT 92451-01-9P 283599-55-3P 283599-58-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(polymeric delivery agents comprising polymer conjugated to modified
amino acid or derivative thereof)
RN 92451-01-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-
oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



RN 283599-55-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[8-[(2-hydroxybenzoyl)amino]octyl]am
ino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



RN 283599-58-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[8-[(2-hydroxybenzoyl)amino]octyl]am
ino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2000:475505 CAPLUS Full-text
DOCUMENT NUMBER: 133:109945

TITLE: Polymeric delivery agents comprising a polymer conjugated to a modified amino acid or derivative thereof

INVENTOR(S): Milstein, Sam J.; Barantsevitch, Eugene N.; Wang, Nai Fang; Liao, Jun; Smart, John E.; Conticello, Richard D.; Ottenbrite, Raphael M.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Virginia Commonwealth University

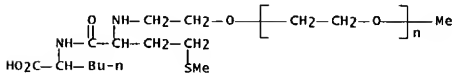
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040203	A2	20000713	WO 2000-US476	20000107 <--
WO 2000040203	A3	20001214		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358463	AA	20000713	CA 2000-2358463	20000107 <--
EP 1146860	A2	20011024	EP 2000-914419	20000107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008590	A	20011030	BR 2000-8590	20000107
JP 2002534363	T2	20021015	JP 2000-591961	20000107
NZ 512581	A	20021220	NZ 2000-512581	20000107
ZA 2001005213	A	20020717	ZA 2001-5213	20010625
US 6627228	B1	20030930	US 2001-889005	20011009
US 2003232085	A1	20031218	US 2003-447608	20030528

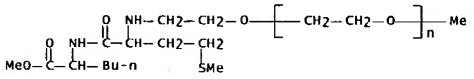
PRIORITY APPLN. INFO.: US 1999-115273P P 19990108
WO 2000-US476 W 20000107
US 2001-889005 A1 20011009

ABSTRACT:
Polymeric delivery agents comprising a polymer conjugated to a modified amino acid or derivative thereof, delivery agent compds. and compns. comprising them which are useful in the delivery of active agents are provided. Poly(N-acryloxysuccinimide) was conjugated with N-(5-aminomethylsalicyloyl)-8-aminocaprylic acid (preparation given). Oral and intracolonic delivery composition comprising human growth hormone and above conjugate was administered to rats. At a dose of 200 mg/kg conjugate, the actual amount of delivery agent dosed was 20 mg/kg. With such a concentration of delivery agent complexed with polymer there was evidence of systemic delivery.

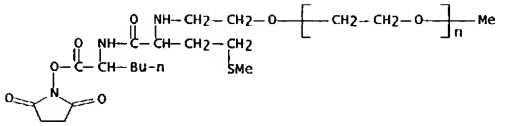
L12 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 274251-41-1DP, conjugates with nonapeptide or insulin 274251-42-2P 274251-43-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for identifying or analyzing polymer linkage sites on macromols. using amino acid report binding)
RN 274251-41-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, ether with N-(2-hydroxyethyl)-L-methionyl-L-norleucine (9CI) (CA INDEX NAME)



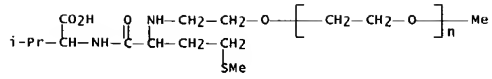
RN 274251-42-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, ether with N-(2-hydroxyethyl)-L-methionyl-L-norleucine methyl ester (9CI) (CA INDEX NAME)



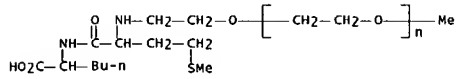
RN 274251-43-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, ether with 1-[[N-(2-hydroxyethyl)-L-methionyl-L-norleucyl]oxy]-2,5-pyrrolidinedione (9CI) (CA INDEX NAME)



IT 274251-40-0P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(method for identifying or analyzing polymer linkage sites on macromols. using amino acid report binding)
RN 274251-40-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, ether with N-(2-hydroxyethyl)-L-methionyl-L-valine (9CI) (CA INDEX NAME)



IT 274251-41-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for identifying or analyzing polymer linkage sites on macromols. using amino acid report binding)
RN 274251-41-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, ether with N-(2-hydroxyethyl)-L-methionyl-L-norleucine (9CI) (CA INDEX NAME)



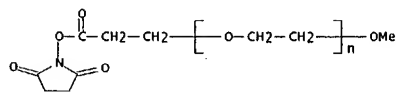
ACCESSION NUMBER: 2000:401439 CAPLUS Full-text
DOCUMENT NUMBER: 133:28273
TITLE: Method for identifying or analyzing polymer linkage sites on macromolecules using amino acid report binding
INVENTOR(S): Schiavon, Oddone; Veronese, Francesco M.; Caliceti, Paolo; Orsolini, Piero
PATENT ASSIGNEE(S): Debio Recherche Pharmaceutique S.A., Switz.
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1008355	A1	20000614	EP 1998-123307	19981208 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2000033881	A1	20000615	WO 1999-IB1957	19991208 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1137442	A1	20011004	EP 1999-973261	19991208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531529	T2	20020924	JP 2000-586371	19991208
AU 757665	B2	20030227	AU 2000-14028	19991208
US 6790942	B1	20040914	US 2001-857469	20010605
PRIORITY APPLN. INFO.:			EP 1998-123307 A	19981208
			WO 1999-IB1957 W	19991208

ABSTRACT:
The aim of the invention is to provide a new method for identifying or analyzing polymer linkage sites on macromols. using amino acid reporter binding. Another aim of this invention is to provide a compound FE ··· L ··· M, where M is a mol. consisting of proteins, peptides or polypeptides, FE is a functionalizing entity and L is a linking arm that is stable under physiol. conditions but cleavable by specific and selective phys.-chemical means. Insulin and lysozyme were each reacted with mPEG-Met-Nle-OSu. The products were analyzed by cleavage with CNBr, chromatog., and mass spectrometry.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

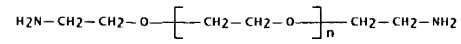
L12 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 174569-25-6DP, reaction products with insulin deriv.
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and characterization of PEG-insulin conjugates)
RN 174569-25-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2000:104754 CAPLUS Full-text
DOCUMENT NUMBER: 132:284063
TITLE: Synthesis and Characterization of Poly(ethylene glycol)-Insulin Conjugates
AUTHOR(S): Hinds, Ken; Koh, Jae Joon; Joss, Lisa; Liu, Feng; Baudys, Miroslav; Kim, Sung Wan
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry/Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Bioconjugate Chemistry (2000), 11(2), 195-201
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Human insulin was modified by covalent attachment of short-chain (750 and 2000 Da) methoxypoly (ethylene glycol) (mPEG) to the amino groups of either residue PheB1 or LysB29, resulting in four distinct conjugates: mPEG(750)-PheB1-insulin, mPEG(2000)-PheB1-insulin, mPEG(750)-LysB29-insulin, and mPEG(2000)-LysB29-insulin. Characterization of the conjugates by MALDI-TOF mass spectrometry and N-terminal protein sequence analyses verified that only a single polymer chain (750 or 2000 Da) was attached to the selected residue of interest (PheB1 or LysB29). Equilibrium sedimentation expts. were performed using anal. ultracentrifugation to quant. determine the association state(s) of insulin derivs. In the concentration range studied, all four of the conjugates and Zn-free insulin exist as stable dimers while Zn2+-insulin was exclusively hexameric and Lispro was monomeric. In addition, insulin (conjugate) self-association was evaluated by CD in the near-UV wavelength range (320-250 nm). This independent method qual. suggests that mPEG-insulin conjugates behave similarly to Zn-free ***insulin*** in the concentration range studied and complements results from ultracentrifugation studies. The phys. stability/resistance to fibrillation of mPEG-insulin conjugates in aqueous solution were assessed. The data proves that mPEG(750 and 2000)-PheB1-insulin conjugates are substantially more stable than controls but the mPEG(750 and 2000)-LysB29-***insulin*** conjugates were only slightly more stable than com. available prepns. CD studies done in the far UV region confirm insulin's tertiary structure in aqueous solution is essentially conserved after mPEG conjugation. In vivo pharmacodynamic assays reveal that there is no loss in biol. activity after conjugation of mPEG(750) to either position on the ***insulin*** B-chain. However, attachment of mPEG(2000) decreased the bioactivity of the conjugates to about 85% of Lilly's HumulinR formulation. The characterization presented in this paper provides strong testimony to the fact that attachment of mPEG to specific amino acid residues of insulin's B-chain improves the conjugates' phys. stability without appreciable perturbations to its tertiary structure, self-association behavior, or in vivo biol. activity.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

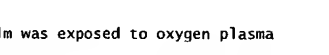
L12 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 24991-53-5DP, Polyethylene glycol diamine, oxidized, reaction products with oxidized PET and biomols.
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(surface characterization and blood compatibility of PET-immobilized with insulin and/or heparin using plasma glow discharge)
RN 24991-53-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-aminoethyl)-ω-(2-aminoethoxy)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2000:41097 CAPLUS Full-text
DOCUMENT NUMBER: 132:212635
TITLE: Surface characterization and in vitro blood compatibility of poly(ethylene terephthalate) immobilized with insulin and/or heparin using plasma glow discharge
AUTHOR(S): Kim, Young Jin; Kang, Inn-Kyu; Huh, Man Woo; Yoon, Sung-Chul
CORPORATE SOURCE: Department of Polymer Science, Kyungpook National University, Taegu, 702-701, S. Korea
SOURCE: Biomaterials (1999), Volume Date 2000, 21(2), 121-130
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Poly(ethylene terephthalate) (PET) film was exposed to oxygen plasma glow discharge to produce peroxides on its surfaces. These peroxides were then used as catalysts for the polymerization of acrylic acid (AA) in order to prepare a carboxylic acid group-introduced PET (PET-AA). Insulin and heparin co-immobilized PET (PET-I-H) was prepared by the grafting of poly(ethylene oxide) (PEO) on to PET-AA, followed by reaction first with insulin and then heparin. These surface-modified PETs were characterized by attenuated total reflection FT-IR spectroscopy, ESCA, and a contact angle goniometer. The concentration of the heparin (1.23 μg/cm2) bound to the PEO-grafted PET (PET-PEO) was higher than that (0.77 μg/cm2) on the insulin-immobilized PET (PET-In). The blood compatibilities of the surface-modified PETs were examined using in vitro thrombus formation, plasma recalcification time (PRT), activated partial thromboplastin time (APTT), and platelet adhesion and activation. In the experiment with plasma proteins, the PRT and APTT were significantly prolonged for both the heparin-immobilized PET (PET-He) and the PET-I-H, suggesting the binding of immobilized heparin to antithrombin III. The percentage of platelet adhesion slightly increased with the introduction of AA on the PET surfaces, decreased with the introduction of PEO and insulin, and decreased further with the immobilization of heparin. The release of serotonin was highly suppressed on PET-He and PET-I-H, and on surface-modified PETs the percentage of its release increased with an increase in platelet adhesion.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 31621-87-1, Poly(dioxanone)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled drug delivery system using conjugates of drugs to biodegradable polyesters)
RN 31621-87-1 CAPLUS
CN Poly[oxy(1-oxo-1,2-ethanediyl)oxy-1,2-ethanediyl] (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1999:753037 CAPLUS Full-text
DOCUMENT NUMBER: 132:6348
TITLE: Controlled drug delivery system using the conjugation of drug to biodegradable polyester
INVENTOR(S): Oh, Jong Eun; Lee, Keon Hyoung; Park, Tae Gwan; Nam, Yoon Sung
PATENT ASSIGNEE(S): Mogam Biotechnology Research Institute, S. Korea; Korea Advanced Institute of Science and Technology
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959548	A1	19991125	WO 1999-KR243	19990514 <--

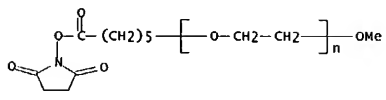
W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 1082105	A1	20010314	EP 1999-919701	19990514
R: CH, DE, ES, FR, GB, IT, LI, SE				
JP 2002526383	T2	20020820	JP 2000-549213	19990514
US 6589548	B1	20030708	US 2000-700380	20001114
US 2004013728	A1	20040122	US 2003-423536	20030425

PRIORITY APPLN. INFO.: KR 1998-17740 A 19980516
WO 1999-KR243 W 19990514
US 2000-700380 A1 20001114
ABSTRACT:
The present invention relates to the mol. sustained controlled release system constructed by the conjugation of mols. to be released with biodegradable polyester polymer via covalent bond and method for preparation thereof. The system may be formulated into microspheres, nanoparticles, or films. The mol. release rate from the above system can be regulated to be proportional to the chemical degradation rate of the biodegradable polyester polymers, resulting in near zero order kinetics profile of release without showing a burst effect. Moreover, the high loading efficiency of hydrophilic drugs can be achieved. FMOC-Trp(Boc) was coupled to poly(glycolic acid-lactic acid), microspheres containing this conjugate prepared, and drug release was studied.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 212969-35-2DP, reaction products with insulin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(chemical modification of insulin with amphiphilic polymers improves intestinal delivery)
RN 212969-35-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-ω-methoxy- (9CI) (CA INDEX NAME)

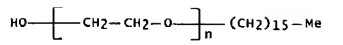


ACCESSION NUMBER: 1998:481722 CAPLUS Full-text
DOCUMENT NUMBER: 129:235492
TITLE: Chemical modification of insulin with amphiphilic polymers improves intestinal delivery
AUTHOR(S): Krishnan, B. Radha; Rajagopalan, J. S.; Anderson, W. L.; Simpson, M.; Ackler, S.; Davis, C. M.; Ansari, A. M.; Harris, T. M.; Ekwuribe, N.
CORPORATE SOURCE: Protein Delivery Inc., Durham, NC, 27713, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 124-125
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Insulin was chemical modified with an amphiphilic polymer that increased its in vitro resistance to GI tract enzymes. A drop in blood glucose and rise in plasma insulin levels from the closed loop studies suggest better intestinal absorption of the modified insulin mixture than native ***insulin.***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 9004-95-9DP, Polyoxyethylene cetyl ether, reaction products with Ara-CMP derivative
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugation-stabilized therapeutic agent compns., delivery and diagnostic formulations)
RN 9004-95-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hexadecyl-ω-hydroxy- (9CI) (CA

INDEX NAME)



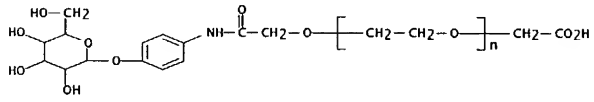
ACCESSION NUMBER: 1997:701459 CAPLUS Full-text
DOCUMENT NUMBER: 128:26913
TITLE: Conjugation-stabilized therapeutic agent compositions, delivery and diagnostic formulations comprising same, and method of making and using the same
INVENTOR(S): Ekwuribe, Nnochiri Nkem
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. 5,438,040.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5681811	A	19971028	US 1995-509422	19950731 <--
US 5359030	A	19941025	US 1993-59701	19930510 <--
US 5438040	A	19950801	US 1994-276890	19940719 <--
CA 2227891	AA	19970213	CA 1996-2227891	19960729 <--
WO 9704796	A1	19970213	WO 1996-US12425	19960729 <--
W: AU, CA, CN, IL, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9666409	A1	19970226	AU 1996-66409	19960729 <--
AU 698944	B2	19981112		
EP 841936	A1	19980520	EP 1996-926169	19960729 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1192690	A	19980909	CN 1996-196079	19960729 <--
JP 11511131	T2	19990928	JP 1996-507838	19960729 <--
US 6191105	B1	20010220	US 1997-958383	19971027
US 2003229006	A1	20031211	US 2003-448524	20030530
US 2003229010	A1	20031211	US 2003-448535	20030602

PRIORITY APPLN. INFO.: US 1993-59701 A3 19930510
US 1994-276890 A2 19940719
US 1995-509422 A 19950731
WO 1996-US12425 W 19960729
US 1997-958383 A3 19971027
US 2000-614203 A1 20000712

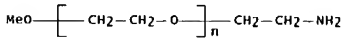
ABSTRACT:
A stabilized conjugated therapeutic agent complex comprising a therapeutic agent conjugatively coupled to a polymer including lipophilic and hydrophilic moieties, wherein the therapeutic agent may for example be selected from the group consisting of insulin, calcitonin, ACTH, glucagon, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic releasing factors, prolactin, thyroid stimulating hormones, endorphins, enkephalins, vasopressin, non-naturally occurring opioids, superoxide dismutase, interferon, asparaginase, arginase, arginine deaminease, adenosine deaminase, RNase, trypsin, chymotrypsin, papain, Ara-A (Arabinofuranosyladenine), Acylguanosine, Nordeoxyguanosine, Azidothymidine, Dideoxyadenosine, Dideoxycytidine, Dideoxyinosine Floxuridine, 6-Mercaptopurine, Doxorubicin, Daunorubicin, or Idarubicin, Erythromycin, Vancomycin, Oleandomycin, Ampicillin; Quinidine and Heparin. In a particular aspect, the invention comprises an insulin composition suitable for parenteral as well as non-parenteral administration, preferably oral or parenteral administration, comprising insulin covalently coupled with a polymer including (i) a linear polyalkylene glycol moiety and (ii) a lipophilic moiety, wherein the insulin, the linear polyalkylene glycol moiety and the lipophilic moiety are conformationally arranged in relation to one another such that the insulin in the composition has an enhanced in vivo resistance to enzymic degradation, relative to insulin alone. One, two, or three polymer constituents may be covalently attached to the therapeutic agent mol., with one polymer constituent being preferred. The ***conjugates*** of the invention are usefully employed in therapeutic as well as non-therapeutic, e.g., diagnostic, applications, and the therapeutic agent and polymer may be covalently coupled to one another, or alternatively may be associatively coupled to one another, e.g., by hydrogen bonding or other associative bonding relationship.

L12 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 194803-11-7DP, reaction products with insulin deriv.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glucose-induced release of glycosylpolyethylene glycol insulin bound to a soluble conjugate of Con A)
RN 194803-11-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-[2-[[4-(α-D-glucopyranosyloxy)phenyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



IT 39927-08-7 80506-64-5D, reaction products with acrylic acid-vinylpyrrolidone copolymer and Con A
RL: RCT (Reactant); RACT (Reactant or reagent)
(glucose-induced release of glycosylpolyethylene glycol insulin bound to a soluble conjugate of Con A)
RN 39927-08-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-(carboxymethoxy)- (9CI) (CA INDEX NAME)

RN 80506-64-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-aminoethyl)-ω-methoxy- (9CI)
(CA INDEX NAME)



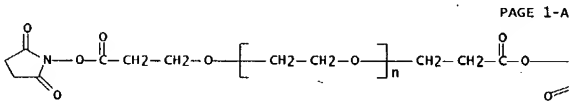
ACCESSION NUMBER: 1997:575511 CAPLUS Full-text
DOCUMENT NUMBER: 127:210259
TITLE: Glucose-Induced Release of Glycosylpoly(ethylene glycol) Insulin Bound to a Soluble Conjugate of Concanavalin A
AUTHOR(S): Liu, Feng; Song, Soo Chang; Mix, Don; Baudys, Miroslav; Kim, Sung Wan
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry/Center for Controlled Chemical Delivery, University Utah, Salt Lake City, UT, 84112, USA
SOURCE: Bioconjugate Chemistry (1997), 8(5), 664-672
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
Treatment of diabetes mellitus by insulin injections provides long-term control of the disease but lacks any feedback response to glucose concentration changes, which finally leads to a number of life-threatening conditions. The purpose of this study was to improve and optimize an implantable, Con A (Con A) based, glucose-responsive insulin delivery system studied earlier [Jeong, S. Y., et al C. (1985)], which can be used for long-term diabetes treatment. To optimize the "insulin component" of the delivery system, we prepared PheB1 insulin amino group monosubstituted monoglucosylpoly(ethylene glycol) (G-PEG) insulin conjugates (PEG Mr 600 or 2000), which showed preserved bioactivity, significantly improved solubility and solution stability at neutral pH, and substantially suppressed hexamerization/dimerization. To improve the delivery system further, we synthesized and characterized a conjugate of Con A and monomethoxypoly(ethylene glycol) (mPEG, Mr 5000) grafted hydrophilic poly(vinylpyrrolidone-co-acrylic acid) (PVPAA) with Mr of 250 000. The optimal ***conjugate*** contained around eight PEG chains and two to three Con A tetramers attached through the amide bonds to the PVPAA chain. The

Con A sugar
binding characteristics were preserved, and, more importantly, Con A solubility at
pH 7.4 substantially increased. This also holds true for a complex formed by
the Con A conjugate and G-PEG insulin, which is soluble and does not precipitate under the physiol. relevant conditions under which the complex
formed by the Con A conjugate and glycosyl insulin immediately ppts. Finally, no leakage of the Con A conjugate from a membrane device was detected. Preliminary in vitro release expts. with Con A
conjugate and G-PEG insulin complex enclosed in the membrane device showed a pulsative, reversible release pattern for G-PEG insulin
in response to glucose challenges of 50-500 mg/dL, demonstrating the feasibility of the release system for use in planned, chronic in vivo studies
with diabetic (pancreatectomized) dogs.

L12 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 123502-57-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(in conjugation of proteins with PEG; fusion proteins and conjugates of leptins with extended in vivo half-lives for control of appetite or weight reduction)
RN 123502-57-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-
oxopropyl]-ω-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropoxy]-(9CI)
(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

ACCESSION NUMBER: 1997:502296 CAPLUS Full-text

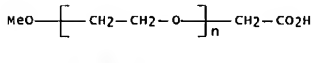
DOCUMENT NUMBER: 127:131002
TITLE: Fusion proteins and conjugates of leptins with extended in vivo half-lives for control of
appetite or weight reduction
INVENTOR(S): De Sauvate, Frederic J.; Levin, Nancy; Vandlen,
Richard L.
PATENT ASSIGNEE(S): Genentech, Inc., USA; De Sauvage, Frederic J.; Levin,
Nancy; Vandlen, Richard L.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9724440	A1	19970710	WO 1996-US20718	19961219 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9610467	A	19980612	ZA 1996-10467	19961212 <--
CA 2238307	AA	19970710	CA 1996-2238307	19961219 <--
AU 9715200	A1	19970728	AU 1997-15200	19961219 <--
EP 870026	A1	19981014	EP 1996-945295	19961219 <--
EP 870026	B1	20040519		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1205738	A	19990120	CN 1996-199265	19961219 <--
BR 9612359	A	19990713	BR 1996-12359	19961219 <--
JP 2000504210	T2	20000411	JP 1997-524551	19961219 <--
NZ 326592	A	20010525	NZ 1996-326592	19961219 <--
RU 2178307	C2	20020120	RU 1998-113706	19961219
AT 267255	E	20040615	AT 1996-945295	19961219
AU 769250	B2	20040122	AU 2001-18291	20010205
AU 2001018291	A5	20011206		

PRIORITY APPLN. INFO.:
US 1995-579494 A 19951227
US 1996-667184 A2 19960620
AU 1997-15200 A3 19961219
WO 1996-US20718 W 19961219

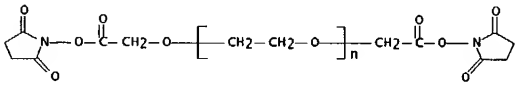
ABSTRACT:
Modified forms of the human Ob gene product (leptin) with extended serum-half-lives are described for use in methods of appetite control or weight
reduction and for treating other physiol. conditions. The invention specifically
concerns leptin fusion protein with Igs and conjugates with polyethylene glycol (PEG). A chimeric gene for a fusion protein of human
leptin and IgG1 was constructed by standard methods and the protein manufactured by
expression of the gene in 293 cells. PEG conjugates were prepared using PEG propionic acid succinimide. Dosage routes were tested in mice and it
was found that a continuous infusion was more effective than daily s.c.
injections.

L12 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 67665-18-3DP, conjugates with insulin
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(bioactive polyethylene glycol-insulin conjugates with enhanced stability)
RN 67665-18-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-methoxy- (9CI)
(CA INDEX NAME)



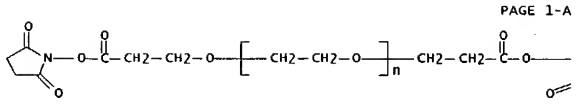
ACCESSION NUMBER: 1997:224421 CAPLUS Full-text
DOCUMENT NUMBER: 126:268416
TITLE: Bioactive polyethylene glycol - insulin conjugates with enhanced stability
AUTHOR(S): Liu, F.; Baudys, M.; Mix, D.; Hinds, K.; Kim, S. W.
CORPORATE SOURCE: Dep. Pharmaceutics Pharmaceutical Chem./CCCD, Univ.
Utah, Salt Lake City, UT, 84112, USA
SOURCE: Polymer Preprints (American Chemical Society, Division
of Polymer Chemistry) (1997), 38(1), 595-596
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer
Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Carboxymethyl methoxy PEG was prepared and conjugated with insulin. The conjugates displayed improved solution stability but the biol. activity delined slightly as the methoxy-PEG moiety mol. weight increased., most
likely explained by nonspecific steric hindrance to the receptor binding by the
methoxy-PEG moiety caused by it large hydrodynamic volume

L12 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 62066-14-2D, collagen conjugates 123502-57-8D, collagen conjugates 159161-70-3D, collagen conjugates 159194-63-5D, collagen conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)
RN 62066-14-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-
oxoethyl]-ω-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethoxy]-(9CI)
(CA INDEX NAME)



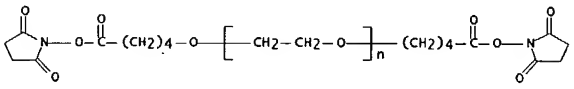
RN 123502-57-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-
oxopropyl]-ω-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropoxy]-(9CI)
(CA INDEX NAME)

PAGE 1-A

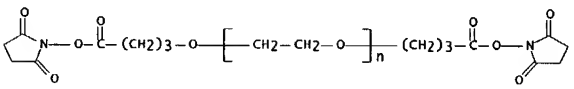


PAGE 1-B

RN 159161-70-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-
oxopentyl]-ω-[[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxopentyl]oxy]-
(9CI) (CA INDEX NAME)



RN 159194-63-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-
oxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]-
(9CI)
(CA INDEX NAME)



ACCESSION NUMBER: 1994:708312 CAPLUS Full-text

DOCUMENT NUMBER: 121:308312
TITLE: Collagen-polymer conjugates for nonimmunogenic compositions and soft tissue augmentation
INVENTOR(S): Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 5,162,430.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5328955	A	19940712	US 1992-922541	19920730 <--
US 5162430	A	19921110	US 1989-433441	19891114 <--
CA 2003538	AA	19900521	CA 1989-2003538	19891121 <--
CA 2003538	C	20010206		
JP 2505312	B2	19960605	JP 1989-501327	19891121 <--
AT 168708	E	19980815	AT 1990-901254	19891121 <--
ES 2119743	T3	19981016	ES 1990-901254	19891121 <--
US 5264214	A	19931123	US 1992-930142	19920814 <--
US 5292802	A	19940308	US 1992-985680	19921202 <--
US 5308889	A	19940503	US 1992-984197	19921202 <--
US 5304595	A	19940419	US 1992-998802	19921230 <--
WO 9401483	A1	19940120	WO 1993-US6292	19930701 <--
W: AU, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346620	A1	19940131	AU 1993-46620	19930701 <--
AU 677789	B2	19970508		
EP 648239	A1	19950419	EP 1993-916926	19930701 <--
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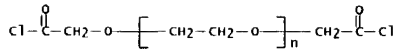
JP 08502082	T2	19960305	JP 1993-503427	19930701 <--
US 5306500	A	19940426	US 1993-110577	19930823 <--
US 5565519	A	19961015	US 1993-147227	19931103 <--
US 5376375	A	19941227	US 1994-177578	19940105 <--
US 5413791	A	19950509	US 1994-198128	19940217 <--
US 5475052	A	19951212	US 1994-236769	19940502 <--
US 5550187	A	19960827	US 1994-287549	19940808 <--
US 5523348	A	19960604	US 1994-292415	19940818 <--
US 5446091	A	19950829	US 1995-368874	19950105 <--
US 5543441	A	19960806	US 1995-427576	19950424 <--
US 5527856	A	19960618	US 1995-440274	19950512 <--
US 5643464	A	19970701	US 1995-497573	19950630 <--
US 5936035	A	19990810	US 1995-573801	19951218 <--
US 5800541	A	19980901	US 1997-780470	19970108 <--

PRIORITY APPLN. INFO.:

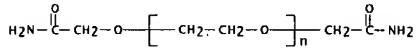
US 1988-274071	B2	19881121
US 1989-433441	A2	19891114
US 1992-907518	A	19920702
US 1992-922541	A2	19920730
US 1992-930142	A3	19920814
US 1992-984197	A	19921202
US 1992-984933	A	19921202
US 1992-985680	A	19921202
US 1993-25032	A	19930302
WO 1993-US6292	A	19930701
US 1993-110577	A3	19930823
US 1993-147227	B2	19931103
US 1994-177578	A3	19940105
US 1994-198128	A2	19940217
US 1994-198812	B1	19940218
US 1994-236769	A2	19940502
US 1994-287549	A3	19940808
US 1994-292415	A3	19940818
US 1995-440863	B1	19950515
US 1995-476825	A2	19950607

ABSTRACT:
Pharmaceutically acceptable, nonimmunogenic compns. are formed by covalently binding atelopeptide collagens to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer ***conjugates.*** The atelopeptide collagen can be type I, II, or III and may be fibrillar or nonfibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivs. thereof having a weight average mol. weight 100-20,000. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amts. of water when formed. The ***conjugates*** can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a nonag. fluid such as an oil and injected for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more. For example, difunctional PEG succinimidyl glutarate was prepared and treated with collagen solution to obtain a microgel of random size fibrils.

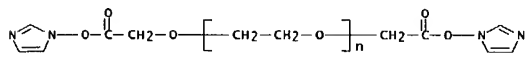
L12 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 35625-91-3D, reaction products with protein or polysaccharide backbone 154623-98-0D, reaction products with protein or polysaccharide backbone 154623-99-1D, reaction products with protein or polysaccharide backbone
RL: BIOL (Biological study)
(biocompatible and biodegradable hydrogel containing, for imaging and therapy)
RN 35625-91-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-chloro-2-oxoethyl)-ω-(2-chloro-2-oxoethoxy)- (9CI) (CA INDEX NAME)



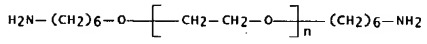
RN 154623-98-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-amino-2-oxoethyl)-ω-(2-amino-2-oxoethoxy)- (9CI) (CA INDEX NAME)



RN 154623-99-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-(1H-imidazol-1-yloxy)-2-oxoethyl]-
ω-[2-(1H-imidazol-1-yloxy)-2-oxoethoxy]- (9CI) (CA INDEX NAME)



IT 123119-57-3
RL: BIOL (Biological study)
(sodium alginate crosslinked with, paramagnetic hydrogel containing)
RN 123119-57-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(6-aminohexyl)-ω-[(6-aminohexyl)oxy]- (9CI) (CA INDEX NAME)

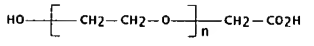


ACCESSION NUMBER: 1994:264829 CAPLUS Full-text
DOCUMENT NUMBER: 120:264829
TITLE: Crosslinked protein or polysaccharide hydrogels, their preparation, and their use in imaging and therapy
INVENTOR(S): Weissleder, Ralph; Bogdanov, Alexei
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

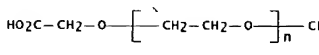
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403155	A1	19940217	WO 1993-US7314	19930804 <--
W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5514379	A	19960507	US 1992-927068	19920807 <--
PRIORITY APPLN. INFO.:			US 1992-927068	A 19920807

ABSTRACT:
Biocompatible, biodegradable hydrogels are prepared from a backbone compound (proteins and polysaccharides, e.g., albumin, polymannuronic acid, or polygalacturonic acid.) bonded to a crosslinking agent. Suitable crosslinking agents include polyvalent derivs. of polyethylene or polyalkylene glycol. These hydrogel compns. may be loaded with diagnostic labels, e.g., radiopaque, paramagnetic, or superparamagnetic materials, or therapeutic drugs, e.g., chemotherapeutic drugs, antibiotics, or cells that produce therapeutic agents. Such hydrogels are used for imaging, treatment, and embolization. Bis(N-hydroxysuccinimidyl)polyethylene glycol disuccinate was prepared and reacted with bovine serum albumin (BSA) and Gd-DTPA-BSA to form a paramagnetic hydrogel. The hydrogel was implanted in rats and the dissoln. was observed by repeated magnetic resonance imaging. Peritoneally implanted samples degraded faster than i.m. implanted samples.

L12 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 39828-93-8P 39927-08-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 39828-93-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 39927-08-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(carboxymethyl)-ω-(carboxymethoxy)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1994:253353 CAPLUS Full-text
DOCUMENT NUMBER: 120:253353
TITLE: Low diol polyalkylene oxide biologically active proteinaceous substances, their preparation, and their medical uses
INVENTOR(S): Snow, Robert A.; Ladd, David L.; Hoyer, Denton W.; Phillips, Christopher P.
PATENT ASSIGNEE(S): Sterling Winthrop Inc., USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

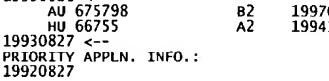
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 584876	A2	19940302	EP 1993-202462	19930821 <--
EP 584876	A3	19940629		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2101361	AA	19940228	CA 1993-2101361	19930727 <--
JP 06172201	A2	19940621	JP 1993-210302	19930825 <--
AU 9344885	A1	19940303	AU 1993-44885	19930826 <--
AU 675798	B2	19970220		
HU 66755	A2	19941228	HU 1993-2440	19930827 <--
PRIORITY APPLN. INFO.:			US 1992-936416	A 19920827

ABSTRACT:
A biol. active proteinaceous composition, comprising a biol. active protein (e.g., interleukin 4, enzymes, peptide hormones) covalently attached to polyalkylene oxide, the polyalkylene oxide having a mol. weight of .apprx.1,000-15,000 Da and being comprised of monomethoxylated and nonmethoxylated polyalkylene oxide such that .ltorsim.10% weight/weight is nonmonomethoxylated polyalkylene oxide, is disclosed, together with a method for its preparation Preferably the low diol polyalkylene oxide is polyethylene glycol having a preferred mol. weight of .apprx.4,000-.apprx.6,000 Da and containing .ltorsim.7% weight/weight nonmethoxylated polyethylene glycol. Also disclosed is a method of treatment of disease processes associated with the adverse effects on tissue of superoxide anions, such as ischemic events, reperfusion injury, trauma and inflammation. Superoxide dismutase (SOD) was conjugated with low diol methoxypolyethylene glycol N-succinimidyl succinate (preparation given). The low diol conjugate had lower immunogenicity than that of high diol PEG-SOD and was also more stable.

L12 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 139204-67-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with carbomethoxycarbonylsulfenyl chloride)
RN 139204-67-4 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-carboxy-1-oxo[(triphenylmethyl)thio]propyl]amino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)

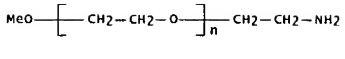
CM 1

CRN 95436-20-7
CMF C23 H20 O4 S



CM 2

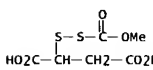
CRN 80506-64-5
CMF (C2 H4 O)n C3 H9 N O
CCI PMS



IT 139204-69-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with isopropylthiol)
RN 139204-69-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-carboxy[(methoxycarbonyl)dithio]-1-oxopropyl]amino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)

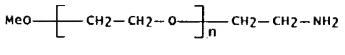
CM 1

CRN 139204-68-5
CMF C6 H8 O6 S2



CM 2

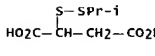
CRN 80506-64-5
CMF (C2 H4 O)n C3 H9 N O
CCI PMS



IT 139249-26-6P
RL: PREP (Preparation)
(preparation of, for targeting delivery in biol. systems)
RN 139249-26-6 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-carboxy[(1-methylethyl)dithio]-1-oxopropyl]amino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)

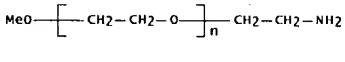
CM 1

CRN 139249-25-5
CMF C7 H12 O4 S2



CM 2

CRN 80506-64-5
CMF (C2 H4 O)n C3 H9 N O
CCI PMS



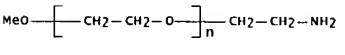
ACCESSION NUMBER: 1992:262511 CAPLUS Full-text
DOCUMENT NUMBER: 116:262511
TITLE: Conjugate compounds of polymers with organic compounds as inert carriers in biological systems
INVENTOR(S): Schacht, Etienne Honore; Duncan, Ruth; Loccufier, Johan
PATENT ASSIGNEE(S): Belg.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9115242	A1	19911017	WO 1991-GB515	19910402 <--
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9175638	A1	19911030	AU 1991-75638	19910402 <--
GB 2244491	A1	19911204	GB 1991-6894	19910402 <--

PRIORITY APPLN. INFO.: GB 1990-7384 19900402
WO 1991-GB515 19910402

ABSTRACT:
Conjugate compds. which have particularly useful applications in biol. systems, e.g. as drug delivery agents containing site-specific targeting moieties, are prepared by coupling of organic mol. entities to polymers having SH-specific reactive groups. Thus, 2-(S-trityl)mercaptoethylamine was reacted with chloroformate-activated dextran to give S-trityl-substituted dextran, which was subsequently treated with methoxycarbonyl sulfenyl chloride. The resulting methoxycarbonyl disulfide derivative was isolated and the reactivity of the compound was evaluated using iso-Pr thiol and reduced glutathione as model thiol-containing compds.

L12 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 80506-64-5DP, derivs., conjugates with proteins
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as drugs with improved stability and long-lasting activity)
RN 80506-64-5 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-aminoethyl)-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1992:256064 CAPLUS Full-text
DOCUMENT NUMBER: 116:256064
TITLE: Stabilization of somatotropins and other proteins by modification of cysteine residues
INVENTOR(S): Buckwalter, Brian Lee; Cady, Susan Mancini; Daley, Michael Joseph; Shieh, Hong Ming
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

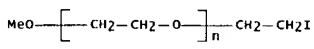
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 458064	A2	19911127	EP 1991-106224	19910418 <--
EP 458064	A3	19920617		
EP 458064	B1	19980225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 163431	E	19980315	AT 1991-106224	19910418 <--
ES 2113354	T3	19980501	ES 1991-106224	19910418 <--
IL 97932	A1	19980222	IL 1991-97932	19910424 <--
AU 9176075	A1	19911107	AU 1991-76075	19910429 <--
AU 639324	B2	19930722		
CA 2041742	AA	19911105	CA 1991-2041742	19910502 <--
JP 06009696	A2	19940118	JP 1991-128190	19910502 <--
NO 9101752	A	19911105	NO 1991-1752	19910503 <--
FI 9102144	A	19911105	FI 1991-2144	19910503 <--
ZA 9103359	A	19920325	ZA 1991-3359	19910503 <--
US 5951972	A	19990914	US 1995-383621	19950206 <--
US 6010999	A	20000104	US 1995-459906	19950602 <--

PRIORITY APPLN. INFO.: US 1990-519047 19900504
EP 1991-106224 19910418
US 1991-766142 19910925
US 1995-383621 19950206

ABSTRACT:
Physiol.-active natural and recombinant mammalian and human proteins or polypeptides containing cysteine residues are chemical modified at the cysteine residues by derivatizing compds. ZCH2CO2R1, ZCH2CONHCH(COR2)[(CH2)xCOR3], ZCH(COR2)[(CH2]xCOR3], or ZCH2CONH(CH2)xCOR2 [R1 = CH2CH2(OCH2CH2)yOMe; R2, R3 = H, NHCH2CH2(OCH2CH2)yOMe, OCH2CH2(OCH2CH2)yOMe; Z = Br, I; x = 1-3; y = 10-300; R2, R3 simultaneously ≠ H]. Preferred proteins or polypeptides include somatotropins, interleukins, interferons, prourokinases, IGF-1s, IGF-2s, growth factors such as fibroblast growth factor, and antithrombin III.

when the derivatized proteins or polypeptides are formulated, they provide
improved stable, long-acting pharmaceutical compns., previously difficult to
achieve. Thus, to a solution of 400 mg recombinant porcine somatotropin (rpST)
(I) in 200 mL 0.5M NH4HCO3 (pH 8.4) was added 28.0 mg dithiothreitol and the
mixture was stirred for 1 h. To this reduced I was added 1g ICH2CO-Asp-NH-PEG-
OMe (II; PEG = polyethylene glycol residue) (preparation given) and after stirring
the mixture for 3 h, an addnl. 1 g II was added and stirring was continued for 18
h to give 400 mg [Cys(Q)183.191]-rpST (Q = CH2CO-Asp-NH-PEG-OMe) (III). III at
80 μg/day for 10 days showed a total weight gain of 31.4 g in hypophysectomized
albino rats vs. 28.0 g when rpST was administered.

L12 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 134141-55-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and alkylation by, of dihydroxyacetophenone)
RN 134141-55-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-iodoethyl)-ω-methoxy- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1991:247792 CAPLUS Full-text
DOCUMENT NUMBER: 114:247792
TITLE: Preparation of polyethylene glycol phenylglyoxal
derivatives for modification of peptides
INVENTOR(S): Ono, Keiichi; Kai, Yoshiyuki; Ikeda, Yoshiharu; Maeda, Hiroo
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 400486	A2	19901205	EP 1990-109907	19900524 <--
EP 400486	A3	19910626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 03088822	A2	19910415	JP 1990-90637	19900404 <--
JP 2997004	B2	20000111		
CA 2017541	AA	19901126	CA 1990-2017541	19900525 <--

PRIORITY APPLN. INFO.: JP 1989-134226 A 19890526
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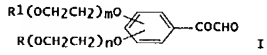
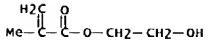


ABSTRACT:
Polyethylene glycol phenylglyoxal derivs. I (R, R1 = lower alkyl, n, m = same
or different integer such that the average mol. weight is 1000-12,000) were prepared for
modification of the guanidino groups in peptides. Thus, tosylation of
monomethoxypolyethylene glycol and substitution with NaI gave iodide
Me(OCH2CH2)n I (II). Alkylation of 3,5-(HO)2C6H3COMe with II followed by
oxidation with SeO2 gave phenylglyoxal derivs. I (R = R1 = Me). I (R = R1 = Me)
were used to modify arginine-containing peptides superoxide dismutase,
insulin -like growth factors I and II, calcitonin gene related peptide,
and elastase.

L12 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
IT 88285-53-4P, Glycidyl methacrylate-2-hydroxyethyl methacrylate-triethyleneglycol dimethacrylate copolymer
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for light-scattering assay)
RN 88285-53-4 CAPLUS
CN 2-Propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester,
polymer with 2-hydroxyethyl 2-methyl-2-propenoate and oxiranylmethyl
2-methyl-2-propenoate (9CI) (CA INDEX NAME)

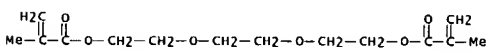
CM 1

CRN 868-77-9
CMF C6 H10 O3



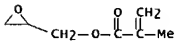
CM 2

CRN 109-16-0
CMF C14 H22 O6



CM 3

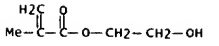
CRN 106-91-2
CMF C7 H10 O3



IT 88285-53-4DP, Glycidyl methacrylate-2-hydroxyethyl methacrylate-triethyleneglycol dimethacrylate copolymer, conjugates with anti-swine insulin antiserum
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for light-scattering immunoassay for insulin)
RN 88285-53-4 CAPLUS
CN 2-Propenoic acid, 2-methyl-, 1,2-ethanediylbis(oxy-2,1-ethanediyl) ester,
polymer with 2-hydroxyethyl 2-methyl-2-propenoate and oxiranylmethyl
2-methyl-2-propenoate (9CI) (CA INDEX NAME)

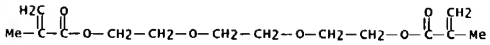
CM 1

CRN 868-77-9
CMF C6 H10 O3



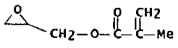
CM 2

CRN 109-16-0
CMF C14 H22 O6



CM 3

CRN 106-91-2
CMF C7 H10 O3



ACCESSION NUMBER: 1989:150959 CAPLUS Full-text
DOCUMENT NUMBER: 110:150959
TITLE: Method of assaying biologically active substances and
fine particle labeling agents therefor
INVENTOR(S): Uchida, Takafumi; Hosaka, Shuntaro
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: U.S., 15 pp. Cont. of U.S. Ser. No. 397,080, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4792527	A	19881220	US 1985-707171	19850228 <--
JP 58014057	A2	19830126	JP 1981-110896	19810717 <--

PRIORITY APPLN. INFO.: JP 1981-110896 19810717

JP 1981-158183

19811006

US 1982-397080

19820712

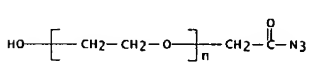
ABSTRACT:
Biol. active substances are assayed by a competitive method or by a sandwich technique in which the labeling agent comprises hydrophilic fine particles of 0.03-3 μm bound to analyte or to analyte binding partner, resp., and labeled substance remaining in solution is measured. A solid phase for an insulin immunoassay was prepared by polymerizing glycidyl methacrylate, 2-hydroxyethyl methacrylate, and triethylene glycol dimethacrylate in a molar ratio of 85.7:9.5:4.8, aminating, hydrolyzing, activating the resulting fine particles (4.3 μm) with glutaraldehyde, and reacting them with anti-swine ***insulin*** antiserum and then with bovine serum albumin. Labeled ***insulin*** was prepared by reacting swine insulin with activated fine particles comprising glycidyl methacrylate, methacrylate, and ethylene glycol dimethacrylate (85:10:5 molar ratio; 0.27 μm). The solid phase fine particles were reacted with solns. containing varying amts. of swine ***insulin*** for 2 h and then overnight with active fine particle-fixed ***insulin.*** The mixture was centrifuged at 3000 rpm for 5 min to sediment the solid phase and active fine particles combined with the solid phase. The light-scattering intensity of the dispersion of unreacted fine particles in the supernatant was measured at 400 nm with a spectrofluorometer. Insulin was determined at 25-6.25 microunits/mL.

L12 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

IT 58914-57-1P
RL: PRP (Properties); PREP (Preparation)
(preparation and conjugation of, with enzymes or polypeptides, for nonimmunogenic prepns.)

RN 58914-57-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-(2-azido-2-oxoethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 58914-55-9 CAPLUS

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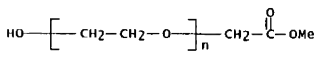
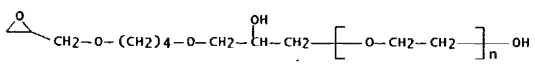


IT 73342-21-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with insulin, for nonimmunogenic prepns.)

RN 73342-21-9 CAPLUS

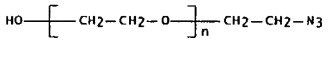
CN Poly(oxy-1,2-ethanediyl), α-[2-hydroxy-3-[4-(oxiranylmethoxy)butoxy]propyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IT 73342-16-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reduction of)

RN 73342-16-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-(2-azidoethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



IT 32130-27-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with maleic anhydride)

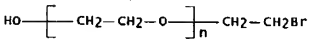
RN 32130-27-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-(2-aminoethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)

IT 73342-17-3P
RL: PREP (Preparation)
(preparation and conversion to azide)

RN 73342-17-3 CAPLUS

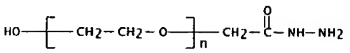
CN Poly(oxy-1,2-ethanediyl), α-(2-bromoethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



IT 58914-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and diazotization of)

RN 58914-56-0 CAPLUS

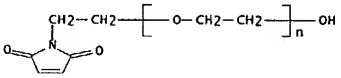
CN Poly(oxy-1,2-ethanediyl), α-(2-hydrazino-2-oxoethyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



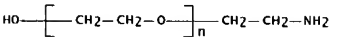
IT 58914-60-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with cholesterol hydroxylation)

RN 58914-60-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IT 58914-55-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with hydrazine)



ACCESSION NUMBER: 1980:185910 CAPLUS Full-text
DOCUMENT NUMBER: 92:185910
TITLE: Nonimmunogenic polypeptides
INVENTOR(S): Davis, Frank F.; Van Es, Theodorus; Palczuk, Nicholas C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

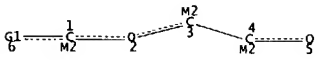
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4179337	A	19791218	US 1977-819831	19770728 <--
PRIORITY APPLN. INFO.:			US 1973-381191	19730720
			US 1975-596931	19750717

ABSTRACT:
Polypeptides such as enzymes or insulin are coupled to polyethylene glycol (PEG) or polypropylene glycol to give a phys. active nonimmunogenic water for polypeptide composition The glycols protect the peptides from loss of activity and the composition can be injected with no immunogenic response. Thus, PEG 750 [25322-68-3] or PEG 2000 was dissolved in anhydrous C6H6 containing Na2CO3. The solution was cooled and cyanuric chloride [108-77-0] was added to give PEG 4-hydroxy-6-chloro-1,3,5-triazine (I) [58914-58-2]. I was added to ***insulin*** , dissolved in 0.1 M borate buffer, pH 9.2, to give a PEG-4-hydroxy-1,3,5-triazin-6-yl conjugate (II). II had ***insulin*** activity of .apprx.50% of insulin activity when injected into rabbits based on weight of conjugated insulin administered. II also had no antigenic activity visavis insulin antiserum.

=> d l2
L2 HAS NO ANSWERS
L2 STR

C7 O8 S9 N10

Page 1-A



Page 1-B
VAR G1=7/8/9/10
NODE ATTRIBUTES:
HCOUNT IS M2 AT 1
HCOUNT IS M2 AT 3
HCOUNT IS M2 AT 4
NSPEC IS C AT 1
NSPEC IS C AT 2
NSPEC IS C AT 3
NSPEC IS C AT 4
NSPEC IS C AT 5
NSPEC IS C AT 6
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 2 3 4 5 7 8 9 10
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	146.35	301.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-16.80	16.80

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

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LAST RELOADED: Sep 17, 2004 (20040917/UP).

=> DIS HIST

(FILE 'HOME' ENTERED AT 14:21:11 ON 23 SEP 2004)

FILE 'REGISTRY' ENTERED AT 14:21:16 ON 23 SEP 2004
L1 SCREEN 2043
L2 STRUCTURE UPLOADED
L3 QUE L2 AND L1
L4 64914 S L3 FUL

FILE 'CAPLUS' ENTERED AT 14:21:51 ON 23 SEP 2004
L5 71947 L4
L6 287 L5 AND INSULIN
L7 245 L6 AND ENGLISH/LA
L8 136 L7 AND PATENT/DT
L9 109 L7 NOT L8
L10 74 L8 AND PD<20010215
L11 164 L7 AND PD<20010215
L12 24 L11 AND CONJUGATE

FILE 'STNGUIDE' ENTERED AT 14:28:32 ON 23 SEP 2004

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.30	302.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	16.80

STN INTERNATIONAL LOGOFF AT 14:31:34 ON 23 SEP 2004

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Welcome to STN International!  Enter x:x

LOGINID:ssspta1653adk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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* *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12  BEILSTEIN enhanced with new display and select
options,
                  resulting in a closer connection to BABS
 NEWS  4  Jul 30  BEILSTEIN on STN workshop to be held August 24 in
conjunction
                  with the 228th ACS National Meeting
 NEWS  5  AUG 02  IFIPAT/IFIUDB/IFICDB reloaded with new search and
display
                  fields
 NEWS  6  AUG 02  CAplus and CA patent records enhanced with European
and Japan
                  Patent Office Classifications
 NEWS  7  AUG 02  The Analysis Edition of STN Express with Discover!
                  (Version 7.01 for Windows) now available
 NEWS  8  AUG 04  Pricing for the Save Answers for SciFinder Wizard
within
                  STN Express with Discover! will change September 1,
2004
 NEWS  9  AUG 27  BIOCOMMERCE: Changes and enhancements to content
coverage
 NEWS 10  AUG 27  BIOTECHABS/BIOTECHDS: Two new display fields added
for legal
                  status data from INPADOC
 NEWS 11  SEP 01  INPADOC: New family current-awareness alert (SDI)
available
 NEWS 12  SEP 01  New pricing for the Save Answers for SciFinder
Wizard within
                  STN Express with Discover!
 NEWS 13  SEP 01  New display format, HITSTR, available in
WPIDS/WPINDEX/WPIX
 NEWS 14  SEP 14  STN Patent Forum to be held October 13, 2004, in
Iselin, NJ

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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* *

FILE 'HOME' ENTERED AT 15:25:44 ON 23 SEP 2004

=> FIL REGISTRY
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL                                                  ENTRY

SESSION
FULL ESTIMATED COST                                       0.21
0.21

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STRUCTURE FILE UPDATES:   22 SEP 2004  HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES:  22 SEP 2004  HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
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Experimental and calculated property data are now available. For more
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to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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Uploading H:\STN queries\10075097d.str
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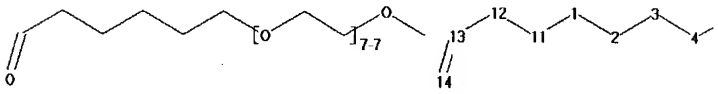


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1  2  3  4  5  6  7  8  11  12  13  14
chain bonds :
1-2  1-11  2-3  3-4  4-5  5-6  6-7  7-8  11-12  12-13  13-14
exact/norm bonds :
3-4  4-5  6-7  7-8  13-14
exact bonds :
1-2  1-11  2-3  5-6  11-12  12-13

Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS
8:CLASS  11:CLASS  12:CLASS  13:CLASS  14:CLASS


L1      STRUCTURE UPLOADED

=> s l1 sam
SAMPLE SEARCH INITIATED 15:26:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   2734 TO ITERATE

 36.6% PROCESSED    1000 ITERATIONS                              1
ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       51544 TO     57816
PROJECTED ANSWERS:              1 TO       153

L2            1 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 15:26:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  55952 TO ITERATE

100.0% PROCESSED   55952 ITERATIONS                             7
ANSWERS
SEARCH TIME: 00.00.01

L3            7 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE
TOTAL                                            ENTRY

SESSION
FULL ESTIMATED COST                                  155.42
155.63

FILE 'CAPLUS' ENTERED AT 15:26:19 ON 23 SEP 2004
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FILE COVERS 1907 - 23 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004  (20040922/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            13 L3

=> l4 and insulin
         166064 INSULIN
           5184 INSULINS
         166144 INSULIN
                (INSULIN OR INSULINS)
L5             9 L4 AND INSULIN

=> d l5 1-9 hitstr ibib abs

L5   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
IT   502487-21-0D, conjugates with human insulin
     RL: BSU (Biological study, unclassified); PAC (Pharmacological
activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical compns. of insulin drug-oligomer conjugates
        for treating diseases)
RN   502487-21-0  CAPLUS
CN   2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid (9CI)  (CA
INDEX NAME)
```

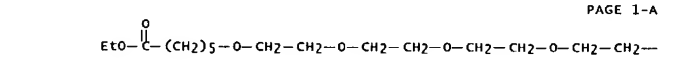

MeO—CH2—CH2—O—CH2—CH2—O—CH2—CH2—O—CH2—CH2—O—CH2—CH2—O—

PAGE 1-B

—CH2—CH2—O—CH2—CH2—O—(CH2)5—CO2H

IT 502487-20-9P 502487-21-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(pharmaceutical compns. of insulin drug-oligomer conjugates for treating diseases)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

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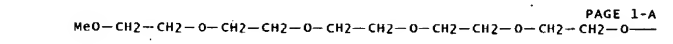
RN 502487-21-0 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

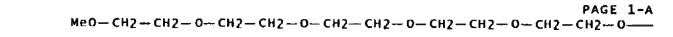
—CH2—CH2—O—CH2—CH2—O—(CH2)5—CO2H

IT 502487-22-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(pharmaceutical compns. of insulin drug-oligomer conjugates for treating diseases)
RN 502487-22-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-
yl)oxy]- (9CI) (CA INDEX NAME)

OTHER SOURCE(S): MARPAT 140:193075
AB Pharmaceutical compns. that include insulin, an insulin drug-oligomer conjugate, a fatty acid component, and a bile salt component or a bile salt component without a fatty acid component are described. The insulin drug is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component, when together, can be present in a weight-to-weight ratio of between 1:15 and 15:1. Methods of treating an insulin deficiency in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. Substantial redns. in blood glucose were observed as the result of coadministration of hexyl- insulin monoconjugate 2 (HIM2) and bile salts to mice and dogs. All of the bile salts were effective at a level of 1.5 %.

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 502487-21-0D, conjugates with insulin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral insulin-oligomer conjugate for reducing hypoglycemic episodes in treatment of diabetes mellitus)
RN 502487-21-0 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—CH2—CH2—O—CH2—CH2—O—(CH2)5—CO2H

ACCESSION NUMBER: 2003:1006707 CAPLUS Full-text
DOCUMENT NUMBER: 140:35957
TITLE: Methods of reducing hypoglycemic episodes in the treatment of diabetes mellitus by orally administering an insulin-oligomer conjugate
INVENTOR(S): Still, James Gordon; Kosutic, Gordana
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105768	A2	20031224	WO 2003-US18763	20030613
WO 2003105768	A3	20040311		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

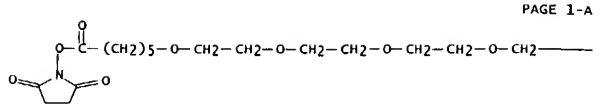
US 2004038867	A1	20040226	US 2003-461199	20030613

PRIORITY APPLN. INFO.: US 2002-388988P P 20020613

OTHER SOURCE(S): MARPAT 140:35957
AB The present invention provides compns. and methods for reducing hypoglycemic episodes experienced by a subject in need of treatment for diabetes mellitus, said method comprising orally administering an amount of an insulin polypeptide-oligomer conjugate to the subject, wherein: (i) the amount of the insulin polypeptide-oligomer conjugate reduces the number and/or severity of hypoglycemic episodes experienced by the subject during a given time period when compared with the number and/or severity of hypoglycemic episodes that would have been experienced during a similar time period by the subject or by subjects in a control group parenterally administered insulin or an insulin analog in an amount that provides a substantially equivalent level of glycemic control; and (ii) the oligomer of the insulin polypeptide-oligomer conjugate comprises a hydrophilic moiety and a lipophilic moiety. Patients with type 1 diabetes were treated p.o. with HIM2 (human insulin with -C(O)(CH2)5(OC2H4)7OCH3 conjugated to the B29 lysine) in comparison with treatment with insulin lispro, s.c. Hypoglycemic events that required rescue intervention were significantly lower in the HIM2 treatment group as compared to the insulin lispro treatment group.

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 502487-20-9P 502487-21-0P 502487-22-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

PAGE 1-A



PAGE 1-B

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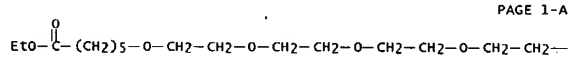
ACCESSION NUMBER: 2004:162445 CAPLUS Full-text
DOCUMENT NUMBER: 140:193075
TITLE: Pharmaceutical compositions of insulin drug-oligomer conjugates and methods of treating diseases therewith
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingam; Ekwuribe, Nnochiri N.; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 235,284.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004038866	A1	20040226	US 2003-382155	20030305
US 2003069170	A1	20030410	US 2002-235284	20020905
US 6770625	B2	20040803		

PRIORITY APPLN. INFO.: US 2001-318193P P 20010907
US 2002-377865P P 20020503
US 2002-235281 A2 20020905
US 2002-235284 A2 20020905

(Reactant or reagent)
(synthesis of insulin polypeptide-oligomer conjugates and proinsulin polypeptide-oligomer conjugates)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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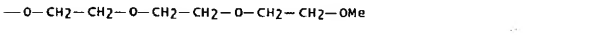

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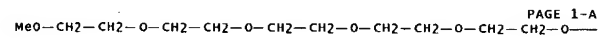
PAGE 1-A



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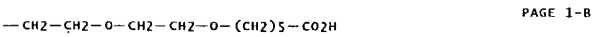
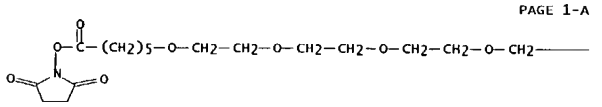


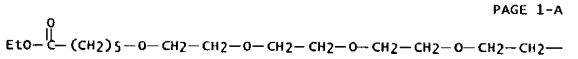
RN 502487-22-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



IT 502487-20-9P 502487-21-0P 502487-22-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis of insulin polypeptide-oligomer conjugates and proinsulin polypeptide-oligomer conjugates)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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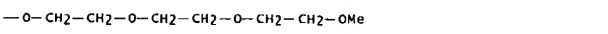

RN 502487-21-0 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid (9CI) (CA INDEX NAME)

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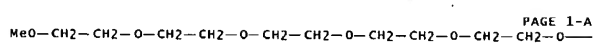

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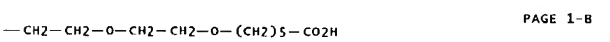

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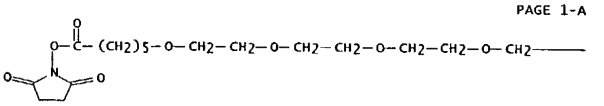
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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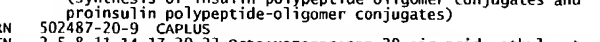

ACCESSION NUMBER: 2003:971710 CAPLUS Full-text
DOCUMENT NUMBER: 140:16981
TITLE: Methods of synthesizing insulin polypeptide-oligomer conjugates and proinsulin polypeptide-oligomer conjugates
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingam; Ekwuribe, Nnochiri N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 101 pp., Cont.-in-part of U.S. Pat. Appl. 2003 87,808.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003229009	A1	20031211	US 2003-382022	20030305
US 2003087808	A1	20030508	US 2001-36744	20011221
US 2003228652	A1	20031211	US 2003-389499	20030317
PRIORITY APPLN. INFO.:			US 2001-318197P	P 20010907
			US 2001-36744	A2 20011221
			US 2003-382022	A2 20030305

OTHER SOURCE(S): MARPAT 140:16981
AB The invention provides a method for synthesizing an insulin polypeptide-oligomer conjugate that includes contacting a proinsulin polypeptide, comprising an insulin polypeptide coupled to one or more peptides by peptide bond(s) capable of being cleaved to yield the insulin polypeptide, with an oligomer under conditions sufficient to couple the oligomer to the insulin polypeptide portion of the proinsulin polypeptide and provide a proinsulin polypeptide-oligomer conjugate, and cleaving the one or more peptides from the proinsulin polypeptide-oligomer conjugate to provide the insulin polypeptide-oligomer conjugate.

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

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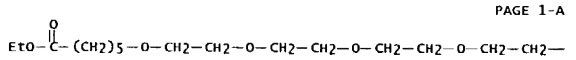
ACCESSION NUMBER: 2003:971618 CAPLUS Full-text
DOCUMENT NUMBER: 140:16980
TITLE: Methods of synthesizing insulin polypeptide-oligomer conjugates and proinsulin polypeptide-oligomer conjugates
INVENTOR(S): Radhakrishnan, Balasingam; Soltero, Richard; Ekwuribe, Nnochiri N.; Puskas, Monica; Sangal, Diti
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 102 pp., Cont.-in-part of U.S. Ser. No. 382,022.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003228652	A1	20031211	US 2003-389499	20030317
US 2003087808	A1	20030508	US 2001-36744	20011221
US 2003229009	A1	20031211	US 2003-382022	20030305
PRIORITY APPLN. INFO.:			US 2001-318197P	P 20010907
			US 2001-36744	A2 20011221
			US 2003-382022	A2 20030305

OTHER SOURCE(S): MARPAT 140:16980
AB The invention provides a method for synthesizing an insulin polypeptide-oligomer conjugate that includes contacting a proinsulin polypeptide, comprising an insulin polypeptide coupled to one or more peptides by peptide bond(s) capable of being cleaved to yield the insulin polypeptide, with an oligomer under conditions sufficient to couple the oligomer to the insulin polypeptide portion of the proinsulin polypeptide and provide a proinsulin polypeptide-oligomer conjugate, and cleaving the one or more peptides from the proinsulin polypeptide-oligomer conjugate to provide the insulin polypeptide-oligomer conjugate.

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 502487-20-9P 502487-21-0P 502487-22-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesizing insulin polypeptide-oligomer conjugates and proinsulin polypeptide-oligomer conjugates)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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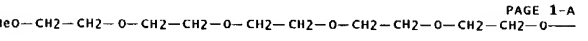

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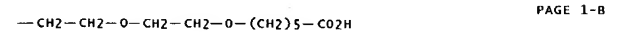

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CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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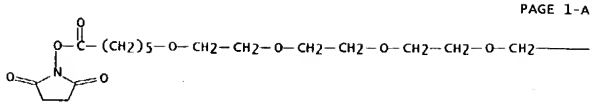

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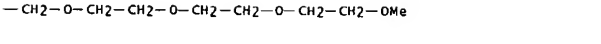


ACCESSION NUMBER: 2003:221806 CAPLUS Full-text
DOCUMENT NUMBER: 138:260413
TITLE: Methods of synthesizing insulin polypeptide-oligomer conjugates, and proinsulin polypeptide-oligomer conjugates and methods of synthesizing same
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingham; Ekwuribe, Nnochiri N.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022996	A2	20030320	WO 2002-US28428	20020906
WO 2003022996	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003087808	A1	20030508	US 2001-36744	20011221
EP 1430082	A2	20040623	EP 2002-766246	20020906

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

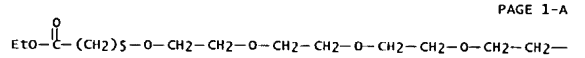
PRIORITY APPLN. INFO.:	US 2001-318197P	P 20010907
	US 2001-36744	A 20011221
	US 2002-349462P	P 20020118
	WO 2002-US28428	W 20020906

OTHER SOURCE(S): MARPAT 138:260413

AB Methods for synthesizing proinsulin polypeptides are described that include a contacting a proinsulin polypeptide including an insulin polypeptide coupled to one or more peptides by peptide bond(s) capable of being cleaved to yield the insulin polypeptide with an oligomer under conditions sufficient to couple the oligomer to the insulin polypeptide portion of the proinsulin polypeptide and provide a proinsulin polypeptide-oligomer conjugate, and cleaving the one or more peptides from the proinsulin polypeptide-oligomer conjugate to provide the insulin polypeptide-oligomer conjugate. Methods of synthesizing proinsulin polypeptide-oligomer conjugates are also described as are proinsulin polypeptide-oligomer conjugates. Methods of synthesizing C-peptide polypeptide-oligomer conjugates are also described.

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 502487-20-9P 502487-21-0P 502487-22-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of oligomers for drug-oligomer conjugates for oral delivery)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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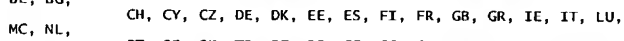

RN 502487-21-0 CAPLUS
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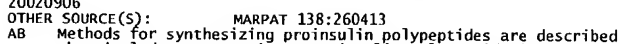
PAGE 1-B



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CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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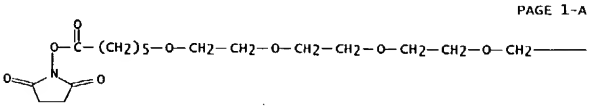

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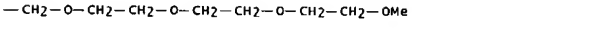

ACCESSION NUMBER: 2003:221462 CAPLUS Full-text
DOCUMENT NUMBER: 138:260437
TITLE: Pharmaceutical compositions of drug-oligomer conjugates for oral administration
INVENTOR(S): Soltero, Richard; Ekwuribe, Nnochiri N.; Opawale, Foyeke; Rehlaender, Bruce; Hickey, Anthony;

Bovet, Li
Li
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022210	A2	20030320	WO 2002-US28536	20020906
WO 2003022210	A3	20031218		

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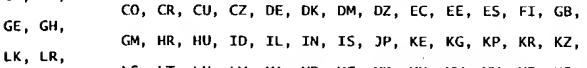
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003083232	A1	20030501	US 2002-235381	20020905
PRIORITY APPLN. INFO.:			US 2001-318193P	P 20010907
			US 2002-377865P	P 20020503

AB An oral pharmaceutical compn. comprising a drug-oligomer conjugate, 0.1-15% of a fatty acid component, and 0.1-15% of a bile salt component is described. The drug, e.g., a peptide or protein, is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1. Methods of treating diseases in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. For example, tablets containing an insulin conjugate HIM2 were prepared by lyophilization of a mixture containing HIM2 2.5 g, Na cholate 30.0 g, oleic acid 10.0 g, 25% sucralose 8.0 g, flavor 4.0 g, capric acid 5.0 g, lauric acid 5.0 g, citric acid 67.2 g, trolamine 42.4 g, NaOH 18.8 g, pH adjusters (5N NaOH and 5N HCl) as needed, and water resulting in an amorphous powder. The powder (127.6 g) was blended with citric acid 29.7 g, sodium citrate 84.2 g, Tris base 106.7 g, microcryst. cellulose 24.8 g, and Explotab 9.4 g and compressed into tablets.

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 502487-20-9P 502487-21-0P 502487-22-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmaceutical compns. of insulin drug-oligomer conjugates)
RN 502487-20-9 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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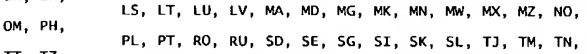
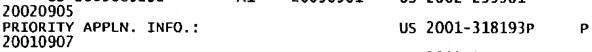


RN 502487-21-0 CAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxanonacosan-29-oic acid (9CI) (CA INDEX NAME)

PAGE 1-A



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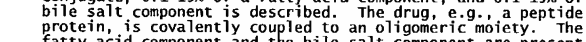
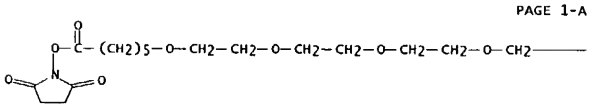


RN 502487-22-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28-octaoxanonacos-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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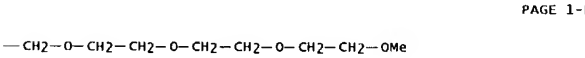


ACCESSION NUMBER: 2003:221460 CAPLUS Full-text
DOCUMENT NUMBER: 138:260435
TITLE: Pharmaceutical compositions of insulin drug-oligomer conjugates
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingham; Ekwuribe, Nnochiri N.; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022208	A2	20030320	WO 2002-US28429	20020906
WO 2003022208	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

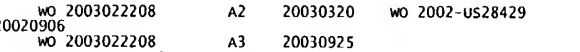
US 2003083232	A1	20030501	US 2002-235381	20020905
PRIORITY APPLN. INFO.:			US 2001-318193P	P 20010907
			US 2002-377865P	P 20020503

OTHER SOURCE(S): MARPAT 138:260435

AB Pharmaceutical compns. that include an insulin drug-oligomer conjugate, a fatty acid component, and a bile salt component are described. The insulin drug is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1. Methods of treating an insulin deficiency in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. E.g., PEG derivs. of fatty acids such as hexanoic acid were prepared, activated and conjugated to insulin derivs.

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 477775-61-4P 477775-62-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in alkylene glycol derivs. preparation; preparation of peptide drug-alkylene glycol oligomer conjugates)
RN 477775-61-4 CAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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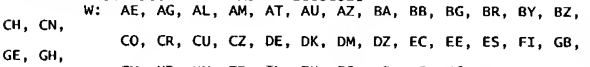

RN 477775-62-5 CAPLUS
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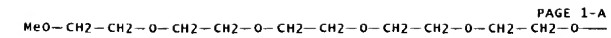
PAGE 1-A



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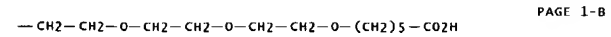
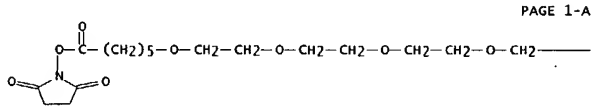


IT 477775-63-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of peptide drug-alkylene glycol oligomer conjugates)
RN 477775-63-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

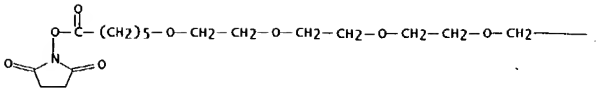
PAGE 1-A



PAGE 1-B

IT 477775-63-6DP, peptide drug conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide drug-alkylene glycol oligomer conjugates)
RN 477775-63-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

ACCESSION NUMBER: 2002:946130 CAPLUS Full-text
DOCUMENT NUMBER: 138:29120
TITLE: Preparation of peptide drug-alkylene glycol oligomer conjugates
INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098446	A1	20021212	WO 2002-US17567	20020604

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003228275	A1	20031211	US 2001-873797	20010604
BR 2001006401	A	20030211	BR 2001-6401	20011011
JP 2003104913	A2	20030409	JP 2001-317307	20011015
EP 1404355	A1	20040407	EP 2002-737357	20020604

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2001-873797	A 20010604
	WO 2002-US17567	W 20020604

OTHER SOURCE(S): MARPAT 138:29120

AB A non-polydispersed mixt. of conjugates in which each conjugate in the mixture comprises a peptide drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixture may exhibit higher in vivo activity than a polydispersed mixture of similar conjugates. The mixture may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixture may result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene solution, followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the conjugate.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
IT 477775-62-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(in alkylene glycol derivs. preparation; preparation of insulin
-alkylene glycol oligomer conjugates)
RN 477775-62-5 CAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

PAGE 1-A

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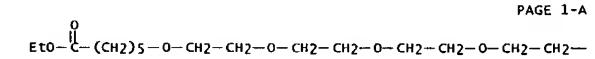
IT 477775-61-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(in alkylene glycol derivs. preparation; preparation of insulin
-alkylene glycol oligomer conjugates)
RN 477775-61-4 CAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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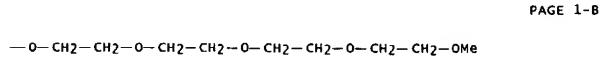
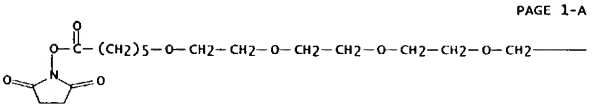


IT 477775-63-6DP, insulin conjugates
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of insulin-alkylene glycol oligomer conjugates)
RN 477775-63-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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IT 477775-63-6
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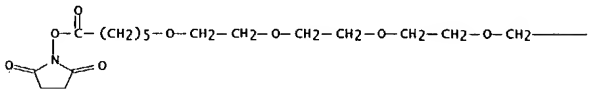
(preparation of insulin-alkylene glycol oligomer conjugates)
RN 477775-63-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

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ACCESSION NUMBER: 2002:946037 CAPLUS Full-text
DOCUMENT NUMBER: 138:16621
TITLE: Preparation of insulin-alkylene glycol oligomer conjugates
INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098232	A1	20021212	WO 2002-US17574	20020604

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003027748	A1	20030206	US 2001-873899 20010604
BR 2001006851	A	20030408	BR 2001-6851 20011011
JP 2003113113	A2	20030418	JP 2001-316998 20011015
EP 1404178	A1	20040407	EP 2002-737359 20020604

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2001-873899	A 20010604
	WO 2002-US17574	W 20020604

OTHER SOURCE(S): MARPAT 138:16621
AB A mixt. of conjugates in which each conjugate in the mixt. comprises an insulin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixture may exhibit higher in vivo activity than a polydispersed mixture of similar conjugates. The mixture may also be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixture may also result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene solution, followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human insulin was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 15:25:49 ON 23 SEP 2004

L1 STRUCTURE UPLOADED
L2 1 S L1 SAM
L3 7 S L1 FUL

FILE 'CAPLUS' ENTERED AT 15:26:19 ON 23 SEP 2004
L4 13 S L3
L5 9 L4 AND INSULIN

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS TOTAL	SINCE FILE ENTRY
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) TOTAL	SINCE FILE ENTRY
SESSION	
CA SUBSCRIBER PRICE	-6.30
	-6.30

STN INTERNATIONAL LOGOFF AT 15:28:32 ON 23 SEP 2004

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15	24	("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730").PN.	USPAT	2004/09/20 11:00
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19	1	(("5889153").PN.) (("5889153").PN.)	USPAT; US-PGPUB	2004/09/20 11:10

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29	35	((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)	USPAT; US-PGPUB	2004/09/20 11:13
30	35	(((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) and ((((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4	USPAT; US-PGPUB	2004/09/20 11:13

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32	1	(((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) and (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4622392"|"4684524"|"4698264"|"4717566"|"4744976"|"4772471"|"4797288"|"4839341"|"4840799"|"4849405"|"4917888"|"4935246"|"4946828"|"4957910"|"4963367"|"4994439"|"5013556"|"5055300"|"5055304"|"5089261"|"5093198"|"5157021"|"5162430"|"5164366"|"5205415"|"5206219"|"5283236"|"5286637"|"5292802"|"5304473"|"5308889"|"5312808"|"5324775"|"5328955"|"5359030"|"5405621"|"5405877"|"5413791"|"5415872"|"5438040"|"5444041"|"5446091"|"5457066"|"5461031"|"5468478"|"5504188"|"550	USPAT; US-PGPUB	2004/09/20 11:16

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34	172	(((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4622392"|"4684524"|"4698264"|"4717566"|"4744976"|"4772471"|"4797288"|"4839341"|"4840799"|"4849405"|"4917888"|"4935246"|"4946828"|"4957910"|"4963367"|"4994439"|"5013556"|"5055300"|"5055304"|"5089261"|"5093198"|"5157021"|"5162430"|"5164366"|"5205415"|"5206219"|"5283236"|"5286637"|"5292802"|"5304473"|"5308889"|"5312808"|"5324775"|"5328955"|"5359030"|"5405621"|"5405877"|"5413791"|"5415872"|"5438040"|"5444041"|"5446091"|"5457066"|"5461031"|"5468478"|"5504188"|"550	USPAT; US-PGPUB	2004/09/20 11:40

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36	1	0566742.pn.	USPAT; US-PGPUB	2004/09/20 11:39
37	172	((((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4622392"|"4684524"|"4698264"|"4717566"|"4744976"|"4772471"|"4797288"|"4839341"|"4840799"|"4849405"|"4917888"|"4935246"|"4946828"|"4957910"|"4963367"|"4994439"|"5013556"|"5055300"|"5055304"|"5089261"|"5093198"|"5157021"|"5162430"|"5164366"|"5205415"|"5206219"|"5283236"|"5286637"|"5292802"|"5304473"|"5308889"|"5312808"|"5324775"|"5328955"|"5359030"|"5405621"|"5405877"|"5413791"|"5415872"|"5438040"|"5444041"|"5446091"|"5457066"|"5461031"|"5468478"|"5504188"|"550	USPAT; US-PGPUB	2004/09/20 11:39

	Hits	Search Text	DBs	Time Stamp
38	173	(((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4622392"|"4684524"|"4698264"|"4717566"|"4744976"|"4772471"|"4797288"|"4839341"|"4840799"|"4849405"|"4917888"|"4935246"|"4946828"|"4957910"|"4963367"|"4994439"|"5013556"|"5055300"|"5055304"|"5089261"|"5093198"|"5157021"|"5162430"|"5164366"|"5205415"|"5206219"|"5283236"|"5286637"|"5292802"|"5304473"|"5308889"|"5312808"|"5324775"|"5328955"|"5359030"|"5405621"|"5405877"|"5413791"|"5415872"|"5438040"|"5444041"|"5446091"|"5457066"|"5461031"|"5468478"|"5504188"|"550	USPAT; US-PGPUB	2004/09/20 11:40
39	173	((((20020160938.pn. 20030144468.pn. 20030087808.pn. 20030083232.pn. 20030069170.pn. 20030060606.pn. 20030050228.pn. 20030027995.pn. 20030004304.pn.) (("4602043"|"4662872"|"4704394"|"4761287"|"4822337"|"4863896"|"4963526"|"5320094"|"5321009"|"5364838"|"5420108"|"5468727"|"5597797"|"5681567"|"5704910"|"5763396"|"5843866"|"5866584"|"5997848"|"6042822"|"6057292"|"6147108"|"6342225"|"6506730"|"5714519").PN.)) (("5889153").PN.)) (("3919411"|"3256153"|"3868356"|"3950517"|"4003792"|"4044196"|"4087390"|"4093574"|"4100117"|"4179337"|"4229438"|"4253998"|"4277394"|"4338306"|"4348387"|"4410547"|"4469681"|"4472382"|"4554101"|"4579730"|"4585754"|"4622392"|"4684524"|"4698264"|"4717566"|"4744976"|"4772471"|"4797288"|"4839341"|"4840799"|"4849405"|"4917888"|"4935246"|"4946828"|"4957910"|"4963367"|"4994439"|"5013556"|"5055300"|"5055304"|"5089261"|"5093198"|"5157021"|"5162430"|"5164366"|"5205415"|"5206219"|"5283236"|"5286637"|"5292802"|"5304473"|"5308889"|"5312808"|"5324775"|"5328955"|"5359030"|"5405621"|"5405877"|"5413791"|"5415872"|"5438040"|"5444041"|"5446091"|"5457066"|"5461031"|"5468478"|"5504188"|"550	USPAT; US-PGPUB	2004/09/20 11:40

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40	2	20030050228.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/20 14:55
41	1	20030050228.pn. and HIM2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/20 15:19
42	8	535930.pn. 5438040.pn. 5681811.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/20 15:01
43	2	535930.pn. 5438040.pn. 5681811.pn.	USPAT; US-PGPUB	2004/09/20 15:01
44	3	5359030.pn. 5438040.pn. 5681811.pn.	USPAT; US-PGPUB	2004/09/20 15:01
45	3	5359030.pn. 5438040.pn. 5681811.pn.	USPAT; US-PGPUB; EPO	2004/09/20 15:04
46	3	(5359030.pn. 5438040.pn. 5681811.pn.) and oral	USPAT; US-PGPUB; EPO	2004/09/20 15:06
47	1	6309633.pn.	USPAT; US-PGPUB; EPO	2004/09/20 15:06
48	1	20030050228.pn. and sugar	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/20 15:20
49	0	10461199.an.	USPAT; US-PGPUB	2004/09/21 10:13
50	0	10166355.an.	USPAT; US-PGPUB	2004/09/21 10:13
51	0	09873797.an.	USPAT; US-PGPUB	2004/09/21 10:13
52	0	10389499.an.	USPAT; US-PGPUB	2004/09/21 10:14
53	0	10389499.pan.	USPAT; US-PGPUB	2004/09/21 10:14
54	4	"10166355"|"09873797"|"10389499"|"10382022"|"10382069"|"10382155"|"10461199".an,pan,pn,pan.	USPAT; US-PGPUB	2004/09/21 10:15